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PTO/SB/05 (2/98)

UTILITY

PATENT APPLICATION
TRANSMITTAL

Attorney Docket No.

210121.427C18

First Inventor or Application Identifier

Jiangchun Xu

Title

COMPOSITIONS AND METHODS FOR THE THERAPY
AND DIAGNOSIS OF PROSTATE CANCER

Express Mail Label No.

EL615232033US

Only for nonprovisional applications under 37 CFR § 1.53(b)

APPLICATION ELEMENTS

See MPEP chapter 600 concerning utility patent application contents.

ADDRESS TO:

Box Patent Application
Assistant Commissioner for Patent
Washington, D.C. 20231

1. ☐ General Authorization Form & Fee Transmittal
(Submit an original and a duplicate for fee processing)

2. ☒ Specification [Total Pages] **216**
(preferred arrangement set forth below)

- Descriptive Title of the Invention
- Cross References to Related Applications
- Statement Regarding Fed sponsored R & D
- Reference to Microfiche Appendix
- Background of the Invention

- Brief Summary of the Invention
- Brief Description of the Drawings (if filed)
- Detailed Description
- Claim(s)
- Abstract of the Disclosure

3. ☒ Drawing(s) (35 USC 113) [Total Sheets] **16**

4. Oath or Declaration [Total Pages] **1**

- a. ☐ Newly executed (original or copy)

- b. ☐ Copy from a prior application (37 CFR 1.63(d))
(for continuation/divisional with Box 17 completed)

- i. ☐ DELETION OF INVENTOR(S)
Signed statement attached deleting
inventor(s) named in the prior application,
see 37 CFR 1.63(d)(2) and 1.33(b)

5. ☐ Incorporation By Reference (useable if box 4b is
checked) The entire disclosure of the prior application,
from which a copy of the oath or declaration is supplied
under Box 4b, is considered to be part of the disclosure of
the accompanying application and is hereby incorporated
by reference therein.

6. ☐ Microfiche Computer Program (Appendix)
7. Nucleotide and Amino Acid Sequence Submission
(if applicable, all necessary)

- a. ☒ Computer-Readable Copy
b. ☒ Paper Copy (identical to computer copy)
c. ☒ Statement verifying identity of above copies

ACCOMPANYING APPLICATION PARTS

8. ☐ Assignment Papers (cover sheet & document(s))
9. ☐ 37 CFR 3.73(b) Statement ☐ Power of Attorney
(when there is an assignee)
10. ☐ English Translation Document (if applicable)
11. ☐ Information Disclosure Statement (IDS)/PTO-1449 ☐ Copies of IDS Citations
12. ☐ Preliminary Amendment
13. ☒ Return Receipt Postcard
14. ☐ Small Entity Statement(s) ☐ Statement filed in prior application, Status still proper and desired
15. ☐ Certified Copy of Priority Document(s)
(if foreign priority is claimed)
16. ☒ Other: Certificate of Express Mail

17. If a CONTINUING APPLICATION, check appropriate box and supply the requisite information below and in a preliminary amendment

☐ Continuation ☐ Divisional ☒ Continuation-In-Part (CIP) of prior Application No.: **09/636,215**

Prior application information: Examiner **not assigned**Group / Art Unit **not assigned**

☐ Claims the benefit of Provisional Application No. _____

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Respectfully submitted,

TYPED or PRINTED NAME Gary M. MylesSIGNATURE Gary M. Myles

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REGISTRATION NO. **46,209**Date August 29, 2000

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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Filed : August 29, 2000

For : COMPOSITIONS AND METHODS FOR THE THERAPY AND
DIAGNOSIS OF PROSTATE CANCER

Docket No. : 210121.427C18

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Box Patent Application
Assistant Commissioner for Patents
Washington, DC 20231

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Assistant Commissioner for Patents:

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Respectfully submitted,

Seed Intellectual Property Law Group PLLC

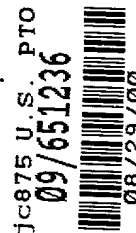

Steve Plante/Jeanette West/Susan Johnson

GMM:sds

Enclosures:

Postcard
Form PTO/SB/05
Specification, Claims, Abstract (216 pages)
16 Sheets of Drawings (Figures 1-12)
Sequence Listing (359 pages)
Declaration for Sequence Listing
Diskette for Sequence Listing

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COMPOSITIONS AND METHODS FOR THE THERAPY
AND DIAGNOSIS OF PROSTATE CANCER

CROSS REFERENCE TO RELATED APPLICATIONS

This application is related to U.S. Patent Application No. 09/636,215, filed
5 August 9, 2000; U.S. Application No. 09/605,783, filed June 27, 2000; U.S. Patent
Application No. 09/593,793, filed June 13, 2000; U.S. Patent Application No. 09/510,737,
filed May 12, 2000; U.S. Patent Application No. 09/568,100, filed May 9, 2000; U.S.
Patent Application No. 09/536,857, filed March 27, 2000; U. S. Patent Application
No. 09/483,672, filed January 14, 2000; U.S. Patent Application No. 09/439,313, filed
10 November 12, 1999; U.S. Patent Application No. 09/352,616, filed July 13, 1999; U.S.
Patent Application No. 09/288,946, filed April 9, 1999; U.S. Patent Application
No. 09/232,149, filed January 15, 1999; U.S. Patent Application No. 09/159,812, filed
September 23, 1998; U.S. Patent Application No. 09/115,453, filed July 14, 1998; U.S.
Patent Application No. 09/030,607, filed February 25, 1998; U.S. Patent Application
15 No. 09/020,956, filed February 9, 1998; U.S. Patent Application No. 08/904,804, filed
August 1, 1997; each a CIP of the previously filed application, and all pending, and U.S.
Patent Application No. 08/806,099, filed February 25, 1997, now abandoned.

TECHNICAL FIELD OF THE INVENTION

The present invention relates generally to therapy and diagnosis of cancer,
20 such as prostate cancer. The invention is more specifically related to polypeptides
comprising at least a portion of a prostate-specific protein, and to polynucleotides encoding
such polypeptides. Such polypeptides and polynucleotides may be used in compositions
for prevention and treatment of prostate cancer, and for the diagnosis and monitoring of
such cancers.

BACKGROUND OF THE INVENTION

Cancer is a significant health problem throughout the world. Although Cancer is a significant health problem throughout the world. Although advances have been made in detection and therapy of cancer, no vaccine or other universally successful method
5 for prevention or treatment is currently available. Current therapies, which are generally based on a combination of chemotherapy or surgery and radiation, continue to prove inadequate in many patients.

Prostate cancer is the most common form of cancer among males, with an estimated incidence of 30% in men over the age of 50. Overwhelming clinical evidence
10 shows that human prostate cancer has the propensity to metastasize to bone, and the disease appears to progress inevitably from androgen dependent to androgen refractory status, leading to increased patient mortality. This prevalent disease is currently the second leading cause of cancer death among men in the U.S.

In spite of considerable research into therapies for the disease, prostate
15 cancer remains difficult to treat. Commonly, treatment is based on surgery and/or radiation therapy, but these methods are ineffective in a significant percentage of cases. Two previously identified prostate specific proteins - prostate specific antigen (PSA) and prostatic acid phosphatase (PAP) - have limited therapeutic and diagnostic potential. For example, PSA levels do not always correlate well with the presence of prostate cancer,
20 being positive in a percentage of non-prostate cancer cases, including benign prostatic hyperplasia (BPH). Furthermore, PSA measurements correlate with prostate volume, and do not indicate the level of metastasis.

In spite of considerable research into therapies for these and other cancers, prostate cancer remains difficult to diagnose and treat effectively. Accordingly, there is a
25 need in the art for improved methods for detecting and treating such cancers. The present invention fulfills these needs and further provides other related advantages.

SUMMARY OF THE INVENTION

Briefly stated, the present invention provides compositions and methods for the diagnosis and therapy of cancer, such as prostate cancer. In one aspect, the present invention provides polypeptides comprising at least a portion of a prostate-specific protein, or a variant thereof. Certain portions and other variants are immunogenic, such that the ability of the variant to react with antigen-specific antisera is not substantially diminished. Within certain embodiments, the polypeptide comprises a sequence that is encoded by a polynucleotide sequence selected from the group consisting of: (a) sequences recited in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823 and 824; (b) variants of a sequence recited in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823 and 824; and (c) complements of a sequence of (a) or (b). In specific embodiments, the polypeptides of the present invention comprise at least a portion of a tumor protein that includes an amino acid sequence selected from the group consisting of sequences recited in SEQ ID NO: 112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534, 537-551, 553-568, 573-586, 588-590, 592, 706-708, 775, 776, 778, 780, 781, 811, 814, 818, 826, 827, 853, 855, 858 and 860-862, and variants thereof.

The present invention further provides polynucleotides that encode a polypeptide as described above, or a portion thereof (such as a portion encoding at least 15 amino acid residues of a prostate-specific protein), expression vectors comprising such polynucleotides and host cells transformed or transfected with such expression vectors.

Within other aspects, the present invention provides pharmaceutical compositions comprising a polypeptide or polynucleotide as described above and a physiologically acceptable carrier.

Within a related aspect of the present invention, immunogenic compositions, or vaccines for prophylactic or therapeutic use are provided. Such

compositions comprise a polypeptide or polynucleotide as described above and an immunostimulant.

The present invention further provides pharmaceutical compositions that comprise: (a) an antibody or antigen-binding fragment thereof that specifically binds to a prostate-specific protein; and (b) a physiologically acceptable carrier.

Within further aspects, the present invention provides pharmaceutical compositions comprising: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) a pharmaceutically acceptable carrier or excipient. Antigen presenting cells include dendritic cells, macrophages, monocytes, fibroblasts and B cells.

Within related aspects, immunogenic compositions, or vaccines, are provided that comprise: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) an immunostimulant.

The present invention further provides, in other aspects, fusion proteins that comprise at least one polypeptide as described above, as well as polynucleotides encoding such fusion proteins.

Within related aspects, pharmaceutical compositions comprising a fusion protein, or a polynucleotide encoding a fusion protein, in combination with a physiologically acceptable carrier are provided.

Compositions are further provided, within other aspects, that comprise a fusion protein, or a polynucleotide encoding a fusion protein, in combination with an immunostimulant.

Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a patient a composition as recited above. The patient may be afflicted with prostate cancer, in which case the methods provide treatment for the disease, or patient considered at risk for such a disease may be treated prophylactically.

The present invention further provides, within other aspects, methods for removing tumor cells from a biological sample, comprising contacting a biological sample with T cells that specifically react with a prostate-specific protein, wherein the step of

contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the protein from the sample.

Within related aspects, methods are provided for inhibiting the development of a cancer in a patient, comprising administering to a patient a biological sample treated as
5 described above.

Methods are further provided, within other aspects, for stimulating and/or expanding T cells specific for a prostate-specific protein, comprising contacting T cells with one or more of: (i) a polypeptide as described above; (ii) a polynucleotide encoding such a polypeptide; and/or (iii) an antigen presenting cell that expresses such a polypeptide;
10 under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells. Isolated T cell populations comprising T cells prepared as described above are also provided.

Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective
15 amount of a T cell population as described above.

The present invention further provides methods for inhibiting the development of a cancer in a patient, comprising the steps of: (a) incubating CD4⁺ and/or CD8⁺ T cells isolated from a patient with one or more of: (i) a polypeptide comprising at least an immunogenic portion of a prostate-specific protein; (ii) a polynucleotide encoding
20 such a polypeptide; and (iii) an antigen-presenting cell that expressed such a polypeptide; and (b) administering to the patient an effective amount of the proliferated T cells, and thereby inhibiting the development of a cancer in the patient. Proliferated cells may, but need not, be cloned prior to administration to the patient.

Within further aspects, the present invention provides methods for
25 determining the presence or absence of a cancer in a patient, comprising: (a) contacting a biological sample obtained from a patient with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; and (c) comparing the amount of polypeptide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient.

Within preferred embodiments, the binding agent is an antibody, more preferably a monoclonal antibody. The cancer may be prostate cancer.

The present invention also provides, within other aspects, methods for monitoring the progression of a cancer in a patient. Such methods comprise the steps of:

- 5 (a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polypeptide detected in step (c) with the amount detected in step
- 10 (b) and therefrom monitoring the progression of the cancer in the patient.

- The present invention further provides, within other aspects, methods for determining the presence or absence of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate-specific protein; (b) detecting in the
- 15 sample a level of a polynucleotide, preferably mRNA, that hybridizes to the oligonucleotide; and (c) comparing the level of polynucleotide that hybridizes to the oligonucleotide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within certain embodiments, the amount of mRNA is detected via polymerase chain reaction using, for example, at least one
 - 20 oligonucleotide primer that hybridizes to a polynucleotide encoding a polypeptide as recited above, or a complement of such a polynucleotide. Within other embodiments, the amount of mRNA is detected using a hybridization technique, employing an oligonucleotide probe that hybridizes to a polynucleotide that encodes a polypeptide as recited above, or a complement of such a polynucleotide.

- 25 In related aspects, methods are provided for monitoring the progression of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate-specific protein; (b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; (c) repeating steps (a) and (b) using a biological sample

obtained from the patient at a subsequent point in time; and (d) comparing the amount of polynucleotide detected in step (c) with the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

Within further aspects, the present invention provides antibodies, such as
 5 monoclonal antibodies, that bind to a polypeptide as described above, as well as diagnostic kits comprising such antibodies. Diagnostic kits comprising one or more oligonucleotide probes or primers as described above are also provided.

These and other aspects of the present invention will become apparent upon reference to the following detailed description and attached drawings. All references
 10 disclosed herein are hereby incorporated by reference in their entirety as if each was incorporated individually.

BRIEF DESCRIPTION OF THE DRAWINGS AND SEQUENCE IDENTIFIERS

Figure 1 illustrates the ability of T cells to kill fibroblasts expressing the representative prostate-specific polypeptide P502S, as compared to control fibroblasts. The
 15 percentage lysis is shown as a series of effector:target ratios, as indicated.

Figures 2A and 2B illustrate the ability of T cells to recognize cells expressing the representative prostate-specific polypeptide P502S. In each case, the number of γ -interferon spots is shown for different numbers of responders. In Figure 2A, data is presented for fibroblasts pulsed with the P2S-12 peptide, as compared to fibroblasts
 20 pulsed with a control E75 peptide. In Figure 2B, data is presented for fibroblasts expressing P502S, as compared to fibroblasts expressing HER-2/*neu*.

Figure 3 represents a peptide competition binding assay showing that the P1S#10 peptide, derived from P501S, binds HLA-A2. Peptide P1S#10 inhibits HLA-A2 restricted presentation of fluM58 peptide to CTL clone D150M58 in TNF release bioassay.
 25 D150M58 CTL is specific for the HLA-A2 binding influenza matrix peptide fluM58.

Figure 4 illustrates the ability of T cell lines generated from P1S#10 immunized mice to specifically lyse P1S#10-pulsed Jurkat A2Kb targets and P501S-

transduced Jurkat A2Kb targets, as compared to EGFP-transduced Jurkat A2Kb. The percent lysis is shown as a series of effector to target ratios, as indicated.

Figure 5 illustrates the ability of a T cell clone to recognize and specifically lyse Jurkat A2Kb cells expressing the representative prostate-specific polypeptide P501S, thereby demonstrating that the P1S#10 peptide may be a naturally processed epitope of the P501S polypeptide.

Figures 6A and 6B are graphs illustrating the specificity of a CD8⁺ cell line (3A-1) for a representative prostate-specific antigen (P501S). Figure 6A shows the results of a ⁵¹Cr release assay. The percent specific lysis is shown as a series of effector:target ratios, as indicated. Figure 6B shows the production of interferon-gamma by 3A-1 cells stimulated with autologous B-LCL transduced with P501S, at varying effector:target ratios as indicated.

Figure 7 is a Western blot showing the expression of P501S in baculovirus.

Figure 8 illustrates the results of epitope mapping studies on P501S.

Figure 9 is a schematic representation of the P501S protein showing the location of transmembrane domains and predicted intracellular and extracellular domains.

Figure 10 is a genomic map showing the location of the prostate genes P775P, P704P, B305D, P712P and P774P within the Cat Eye Syndrome region of chromosome 22q11.2

Figure 11 shows the results of an ELISA assay to determine the specificity of rabbit polyclonal antisera raised against P501S.

Figures 12A(1), 12A(2), 12A(3), and B are the full-length cDNA (SEQ ID NO:591) and predicted amino acid (SEQ ID NO:592) sequences, respectively, for the clone P788P.

SEQ ID NO: 1 is the determined cDNA sequence for F1-13
 SEQ ID NO: 2 is the determined 3' cDNA sequence for F1-12
 SEQ ID NO: 3 is the determined 5' cDNA sequence for F1-12
 SEQ ID NO: 4 is the determined 3' cDNA sequence for F1-16
 SEQ ID NO: 5 is the determined 3' cDNA sequence for H1-1

SEQ ID NO: 6 is the determined 3' cDNA sequence for H1-9
 SEQ ID NO: 7 is the determined 3' cDNA sequence for H1-4
 SEQ ID NO: 8 is the determined 3' cDNA sequence for J1-17
 SEQ ID NO: 9 is the determined 5' cDNA sequence for J1-17
 5 SEQ ID NO: 10 is the determined 3' cDNA sequence for L1-12
 SEQ ID NO: 11 is the determined 5' cDNA sequence for L1-12
 SEQ ID NO: 12 is the determined 3' cDNA sequence for N1-1862
 SEQ ID NO: 13 is the determined 5' cDNA sequence for N1-1862
 SEQ ID NO: 14 is the determined 3' cDNA sequence for J1-13
 10 SEQ ID NO: 15 is the determined 5' cDNA sequence for J1-13
 SEQ ID NO: 16 is the determined 3' cDNA sequence for J1-19
 SEQ ID NO: 17 is the determined 5' cDNA sequence for J1-19
 SEQ ID NO: 18 is the determined 3' cDNA sequence for J1-25
 SEQ ID NO: 19 is the determined 5' cDNA sequence for J1-25
 15 SEQ ID NO: 20 is the determined 5' cDNA sequence for J1-24
 SEQ ID NO: 21 is the determined 3' cDNA sequence for J1-24
 SEQ ID NO: 22 is the determined 5' cDNA sequence for K1-58
 SEQ ID NO: 23 is the determined 3' cDNA sequence for K1-58
 SEQ ID NO: 24 is the determined 5' cDNA sequence for K1-63
 20 SEQ ID NO: 25 is the determined 3' cDNA sequence for K1-63
 SEQ ID NO: 26 is the determined 5' cDNA sequence for L1-4
 SEQ ID NO: 27 is the determined 3' cDNA sequence for L1-4
 SEQ ID NO: 28 is the determined 5' cDNA sequence for L1-14
 SEQ ID NO: 29 is the determined 3' cDNA sequence for L1-14
 25 SEQ ID NO: 30 is the determined 3' cDNA sequence for J1-12
 SEQ ID NO: 31 is the determined 3' cDNA sequence for J1-16
 SEQ ID NO: 32 is the determined 3' cDNA sequence for J1-21
 SEQ ID NO: 33 is the determined 3' cDNA sequence for K1-48
 SEQ ID NO: 34 is the determined 3' cDNA sequence for K1-55

SEQ ID NO: 35 is the determined 3' cDNA sequence for L1-2
 SEQ ID NO: 36 is the determined 3' cDNA sequence for L1-6
 SEQ ID NO: 37 is the determined 3' cDNA sequence for N1-1858
 SEQ ID NO: 38 is the determined 3' cDNA sequence for N1-1860
 5 SEQ ID NO: 39 is the determined 3' cDNA sequence for N1-1861
 SEQ ID NO: 40 is the determined 3' cDNA sequence for N1-1864
 SEQ ID NO: 41 is the determined cDNA sequence for P5
 SEQ ID NO: 42 is the determined cDNA sequence for P8
 SEQ ID NO: 43 is the determined cDNA sequence for P9
 10 SEQ ID NO: 44 is the determined cDNA sequence for P18
 SEQ ID NO: 45 is the determined cDNA sequence for P20
 SEQ ID NO: 46 is the determined cDNA sequence for P29
 SEQ ID NO: 47 is the determined cDNA sequence for P30
 SEQ ID NO: 48 is the determined cDNA sequence for P34
 15 SEQ ID NO: 49 is the determined cDNA sequence for P36
 SEQ ID NO: 50 is the determined cDNA sequence for P38
 SEQ ID NO: 51 is the determined cDNA sequence for P39
 SEQ ID NO: 52 is the determined cDNA sequence for P42
 SEQ ID NO: 53 is the determined cDNA sequence for P47
 20 SEQ ID NO: 54 is the determined cDNA sequence for P49
 SEQ ID NO: 55 is the determined cDNA sequence for P50
 SEQ ID NO: 56 is the determined cDNA sequence for P53
 SEQ ID NO: 57 is the determined cDNA sequence for P55
 SEQ ID NO: 58 is the determined cDNA sequence for P60
 25 SEQ ID NO: 59 is the determined cDNA sequence for P64
 SEQ ID NO: 60 is the determined cDNA sequence for P65
 SEQ ID NO: 61 is the determined cDNA sequence for P73
 SEQ ID NO: 62 is the determined cDNA sequence for P75
 SEQ ID NO: 63 is the determined cDNA sequence for P76

SEQ ID NO: 64 is the determined cDNA sequence for P79

SEQ ID NO: 65 is the determined cDNA sequence for P84

SEQ ID NO: 66 is the determined cDNA sequence for P68

SEQ ID NO: 67 is the determined cDNA sequence for P80 (also referred to

5 as P704P)

SEQ ID NO: 68 is the determined cDNA sequence for P82

SEQ ID NO: 69 is the determined cDNA sequence for U1-3064

SEQ ID NO: 70 is the determined cDNA sequence for U1-3065

SEQ ID NO: 71 is the determined cDNA sequence for V1-3692

10 SEQ ID NO: 72 is the determined cDNA sequence for 1A-3905

SEQ ID NO: 73 is the determined cDNA sequence for V1-3686

SEQ ID NO: 74 is the determined cDNA sequence for R1-2330

SEQ ID NO: 75 is the determined cDNA sequence for 1B-3976

SEQ ID NO: 76 is the determined cDNA sequence for V1-3679

15 SEQ ID NO: 77 is the determined cDNA sequence for 1G-4736

SEQ ID NO: 78 is the determined cDNA sequence for 1G-4738

SEQ ID NO: 79 is the determined cDNA sequence for 1G-4741

SEQ ID NO: 80 is the determined cDNA sequence for 1G-4744

SEQ ID NO: 81 is the determined cDNA sequence for 1G-4734

20 SEQ ID NO: 82 is the determined cDNA sequence for 1H-4774

SEQ ID NO: 83 is the determined cDNA sequence for 1H-4781

SEQ ID NO: 84 is the determined cDNA sequence for 1H-4785

SEQ ID NO: 85 is the determined cDNA sequence for 1H-4787

SEQ ID NO: 86 is the determined cDNA sequence for 1H-4796

25 SEQ ID NO: 87 is the determined cDNA sequence for 1I-4807

SEQ ID NO: 88 is the determined cDNA sequence for 1I-4810

SEQ ID NO: 89 is the determined cDNA sequence for 1I-4811

SEQ ID NO: 90 is the determined cDNA sequence for 1J-4876

SEQ ID NO: 91 is the determined cDNA sequence for 1K-4884

- SEQ ID NO: 92 is the determined cDNA sequence for 1K-4896
- SEQ ID NO: 93 is the determined cDNA sequence for 1G-4761
- SEQ ID NO: 94 is the determined cDNA sequence for 1G-4762
- SEQ ID NO: 95 is the determined cDNA sequence for 1H-4766
- 5 SEQ ID NO: 96 is the determined cDNA sequence for 1H-4770
- SEQ ID NO: 97 is the determined cDNA sequence for 1H-4771
- SEQ ID NO: 98 is the determined cDNA sequence for 1H-4772
- SEQ ID NO: 99 is the determined cDNA sequence for 1D-4297
- SEQ ID NO: 100 is the determined cDNA sequence for 1D-4309
- 10 SEQ ID NO: 101 is the determined cDNA sequence for 1D.1-4278
- SEQ ID NO: 102 is the determined cDNA sequence for 1D-4288
- SEQ ID NO: 103 is the determined cDNA sequence for 1D-4283
- SEQ ID NO: 104 is the determined cDNA sequence for 1D-4304
- SEQ ID NO: 105 is the determined cDNA sequence for 1D-4296
- 15 SEQ ID NO: 106 is the determined cDNA sequence for 1D-4280
- SEQ ID NO: 107 is the determined full length cDNA sequence for F1-12
(also referred to as P504S)
- SEQ ID NO: 108 is the predicted amino acid sequence for F1-12
- SEQ ID NO: 109 is the determined full length cDNA sequence for J1-17
- 20 SEQ ID NO: 110 is the determined full length cDNA sequence for L1-12
(also referred to as P501S)
- SEQ ID NO: 111 is the determined full length cDNA sequence for N1-1862
(also referred to as P503S)
- SEQ ID NO: 112 is the predicted amino acid sequence for J1-17
- 25 SEQ ID NO: 113 is the predicted amino acid sequence for L1-12 (also
referred to as P501S)
- SEQ ID NO: 114 is the predicted amino acid sequence for N1-1862 (also
referred to as P503S)
- SEQ ID NO: 115 is the determined cDNA sequence for P89

SEQ ID NO: 116 is the determined cDNA sequence for P90
 SEQ ID NO: 117 is the determined cDNA sequence for P92
 SEQ ID NO: 118 is the determined cDNA sequence for P95
 SEQ ID NO: 119 is the determined cDNA sequence for P98
 5 SEQ ID NO: 120 is the determined cDNA sequence for P102
 SEQ ID NO: 121 is the determined cDNA sequence for P110
 SEQ ID NO: 122 is the determined cDNA sequence for P111
 SEQ ID NO: 123 is the determined cDNA sequence for P114
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 SEQ ID NO: 126 is the determined cDNA sequence for P124
 SEQ ID NO: 127 is the determined cDNA sequence for P126
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 20 SEQ ID NO: 135 is the determined cDNA sequence for P166
 SEQ ID NO: 136 is the determined cDNA sequence for P176
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 25 SEQ ID NO: 140 is the determined cDNA sequence for P192
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 SEQ ID NO: 142 is the determined cDNA sequence for P204
 SEQ ID NO: 143 is the determined cDNA sequence for P208
 SEQ ID NO: 144 is the determined cDNA sequence for P211

SEQ ID NO: 145 is the determined cDNA sequence for P213
 SEQ ID NO: 146 is the determined cDNA sequence for P219
 SEQ ID NO: 147 is the determined cDNA sequence for P237
 SEQ ID NO: 148 is the determined cDNA sequence for P239
 5 SEQ ID NO: 149 is the determined cDNA sequence for P248
 SEQ ID NO: 150 is the determined cDNA sequence for P251
 SEQ ID NO: 151 is the determined cDNA sequence for P255
 SEQ ID NO: 152 is the determined cDNA sequence for P256
 SEQ ID NO: 153 is the determined cDNA sequence for P259
 10 SEQ ID NO: 154 is the determined cDNA sequence for P260
 SEQ ID NO: 155 is the determined cDNA sequence for P263
 SEQ ID NO: 156 is the determined cDNA sequence for P264
 SEQ ID NO: 157 is the determined cDNA sequence for P266
 SEQ ID NO: 158 is the determined cDNA sequence for P270
 15 SEQ ID NO: 159 is the determined cDNA sequence for P272
 SEQ ID NO: 160 is the determined cDNA sequence for P278
 SEQ ID NO: 161 is the determined cDNA sequence for P105
 SEQ ID NO: 162 is the determined cDNA sequence for P107
 SEQ ID NO: 163 is the determined cDNA sequence for P137
 20 SEQ ID NO: 164 is the determined cDNA sequence for P194
 SEQ ID NO: 165 is the determined cDNA sequence for P195
 SEQ ID NO: 166 is the determined cDNA sequence for P196
 SEQ ID NO: 167 is the determined cDNA sequence for P220
 SEQ ID NO: 168 is the determined cDNA sequence for P234
 25 SEQ ID NO: 169 is the determined cDNA sequence for P235
 SEQ ID NO: 170 is the determined cDNA sequence for P243
 SEQ ID NO: 171 is the determined cDNA sequence for P703P-DE1
 SEQ ID NO: 172 is the predicted amino acid sequence for P703P-DE1
 SEQ ID NO: 173 is the determined cDNA sequence for P703P-DE2

SEQ ID NO: 174 is the determined cDNA sequence for P703P-DE6
 SEQ ID NO: 175 is the determined cDNA sequence for P703P-DE13
 SEQ ID NO: 176 is the predicted amino acid sequence for P703P-DE13
 SEQ ID NO: 177 is the determined cDNA sequence for P703P-DE14
 5 SEQ ID NO: 178 is the predicted amino acid sequence for P703P-DE14
 SEQ ID NO: 179 is the determined extended cDNA sequence for 1G-4736
 SEQ ID NO: 180 is the determined extended cDNA sequence for 1G-4738
 SEQ ID NO: 181 is the determined extended cDNA sequence for 1G-4741
 SEQ ID NO: 182 is the determined extended cDNA sequence for 1G-4744
 10 SEQ ID NO: 183 is the determined extended cDNA sequence for 1H-4774
 SEQ ID NO: 184 is the determined extended cDNA sequence for 1H-4781
 SEQ ID NO: 185 is the determined extended cDNA sequence for 1H-4785
 SEQ ID NO: 186 is the determined extended cDNA sequence for 1H-4787
 SEQ ID NO: 187 is the determined extended cDNA sequence for 1H-4796
 15 SEQ ID NO: 188 is the determined extended cDNA sequence for 1I-4807
 SEQ ID NO: 189 is the determined 3' cDNA sequence for 1I-4810
 SEQ ID NO: 190 is the determined 3' cDNA sequence for 1I-4811
 SEQ ID NO: 191 is the determined extended cDNA sequence for 1J-4876
 SEQ ID NO: 192 is the determined extended cDNA sequence for 1K-4884
 20 SEQ ID NO: 193 is the determined extended cDNA sequence for 1K-4896
 SEQ ID NO: 194 is the determined extended cDNA sequence for 1G-4761
 SEQ ID NO: 195 is the determined extended cDNA sequence for 1G-4762
 SEQ ID NO: 196 is the determined extended cDNA sequence for 1H-4766
 SEQ ID NO: 197 is the determined 3' cDNA sequence for 1H-4770
 25 SEQ ID NO: 198 is the determined 3' cDNA sequence for 1H-4771
 SEQ ID NO: 199 is the determined extended cDNA sequence for 1H-4772
 SEQ ID NO: 200 is the determined extended cDNA sequence for 1D-4309
 SEQ ID NO: 201 is the determined extended cDNA sequence for 1D.1-4278
 SEQ ID NO: 202 is the determined extended cDNA sequence for 1D-4288

SEQ ID NO: 203 is the determined extended cDNA sequence for 1D-4283
 SEQ ID NO: 204 is the determined extended cDNA sequence for 1D-4304
 SEQ ID NO: 205 is the determined extended cDNA sequence for 1D-4296
 SEQ ID NO: 206 is the determined extended cDNA sequence for 1D-4280
 5 SEQ ID NO: 207 is the determined cDNA sequence for 10-d8fwd
 SEQ ID NO: 208 is the determined cDNA sequence for 10-H10con
 SEQ ID NO: 209 is the determined cDNA sequence for 11-C8rev
 SEQ ID NO: 210 is the determined cDNA sequence for 7.g6fwd
 SEQ ID NO: 211 is the determined cDNA sequence for 7.g6rev
 10 SEQ ID NO: 212 is the determined cDNA sequence for 8-b5fwd
 SEQ ID NO: 213 is the determined cDNA sequence for 8-b5rev
 SEQ ID NO: 214 is the determined cDNA sequence for 8-b6fwd
 SEQ ID NO: 215 is the determined cDNA sequence for 8-b6 rev
 SEQ ID NO: 216 is the determined cDNA sequence for 8-d4fwd
 15 SEQ ID NO: 217 is the determined cDNA sequence for 8-d9rev
 SEQ ID NO: 218 is the determined cDNA sequence for 8-g3fwd
 SEQ ID NO: 219 is the determined cDNA sequence for 8-g3rev
 SEQ ID NO: 220 is the determined cDNA sequence for 8-h11rev
 SEQ ID NO: 221 is the determined cDNA sequence for g-f12fwd
 20 SEQ ID NO: 222 is the determined cDNA sequence for g-f3rev
 SEQ ID NO: 223 is the determined cDNA sequence for P509S
 SEQ ID NO: 224 is the determined cDNA sequence for P510S
 SEQ ID NO: 225 is the determined cDNA sequence for P703DE5
 SEQ ID NO: 226 is the determined cDNA sequence for 9-A11
 25 SEQ ID NO: 227 is the determined cDNA sequence for 8-C6
 SEQ ID NO: 228 is the determined cDNA sequence for 8-H7
 SEQ ID NO: 229 is the determined cDNA sequence for JPTPN13
 SEQ ID NO: 230 is the determined cDNA sequence for JPTPN14
 SEQ ID NO: 231 is the determined cDNA sequence for JPTPN23

SEQ ID NO: 232 is the determined cDNA sequence for JPTPN24
 SEQ ID NO: 233 is the determined cDNA sequence for JPTPN25
 SEQ ID NO: 234 is the determined cDNA sequence for JPTPN30
 SEQ ID NO: 235 is the determined cDNA sequence for JPTPN34
 5 SEQ ID NO: 236 is the determined cDNA sequence for PTPN35
 SEQ ID NO: 237 is the determined cDNA sequence for JPTPN36
 SEQ ID NO: 238 is the determined cDNA sequence for JPTPN38
 SEQ ID NO: 239 is the determined cDNA sequence for JPTPN39
 SEQ ID NO: 240 is the determined cDNA sequence for JPTPN40
 10 SEQ ID NO: 241 is the determined cDNA sequence for JPTPN41
 SEQ ID NO: 242 is the determined cDNA sequence for JPTPN42
 SEQ ID NO: 243 is the determined cDNA sequence for JPTPN45
 SEQ ID NO: 244 is the determined cDNA sequence for JPTPN46
 SEQ ID NO: 245 is the determined cDNA sequence for JPTPN51
 15 SEQ ID NO: 246 is the determined cDNA sequence for JPTPN56
 SEQ ID NO: 247 is the determined cDNA sequence for PTPN64
 SEQ ID NO: 248 is the determined cDNA sequence for JPTPN65
 SEQ ID NO: 249 is the determined cDNA sequence for JPTPN67
 SEQ ID NO: 250 is the determined cDNA sequence for JPTPN76
 20 SEQ ID NO: 251 is the determined cDNA sequence for JPTPN84
 SEQ ID NO: 252 is the determined cDNA sequence for JPTPN85
 SEQ ID NO: 253 is the determined cDNA sequence for JPTPN86
 SEQ ID NO: 254 is the determined cDNA sequence for JPTPN87
 SEQ ID NO: 255 is the determined cDNA sequence for JPTPN88
 25 SEQ ID NO: 256 is the determined cDNA sequence for JP1F1
 SEQ ID NO: 257 is the determined cDNA sequence for JP1F2
 SEQ ID NO: 258 is the determined cDNA sequence for JP1C2
 SEQ ID NO: 259 is the determined cDNA sequence for JP1B1
 SEQ ID NO: 260 is the determined cDNA sequence for JP1B2

SEQ ID NO: 261 is the determined cDNA sequence for JP1D3
 SEQ ID NO: 262 is the determined cDNA sequence for JP1A4
 SEQ ID NO: 263 is the determined cDNA sequence for JP1F5
 SEQ ID NO: 264 is the determined cDNA sequence for JP1E6
 5 SEQ ID NO: 265 is the determined cDNA sequence for JP1D6
 SEQ ID NO: 266 is the determined cDNA sequence for JP1B5
 SEQ ID NO: 267 is the determined cDNA sequence for JP1A6
 SEQ ID NO: 268 is the determined cDNA sequence for JP1E8
 SEQ ID NO: 269 is the determined cDNA sequence for JP1D7
 10 SEQ ID NO: 270 is the determined cDNA sequence for JP1D9
 SEQ ID NO: 271 is the determined cDNA sequence for JP1C10
 SEQ ID NO: 272 is the determined cDNA sequence for JP1A9
 SEQ ID NO: 273 is the determined cDNA sequence for JP1F12
 SEQ ID NO: 274 is the determined cDNA sequence for JP1E12
 15 SEQ ID NO: 275 is the determined cDNA sequence for JP1D11
 SEQ ID NO: 276 is the determined cDNA sequence for JP1C11
 SEQ ID NO: 277 is the determined cDNA sequence for JP1C12
 SEQ ID NO: 278 is the determined cDNA sequence for JP1B12
 SEQ ID NO: 279 is the determined cDNA sequence for JP1A12
 20 SEQ ID NO: 280 is the determined cDNA sequence for JP8G2
 SEQ ID NO: 281 is the determined cDNA sequence for JP8H1
 SEQ ID NO: 282 is the determined cDNA sequence for JP8H2
 SEQ ID NO: 283 is the determined cDNA sequence for JP8A3
 SEQ ID NO: 284 is the determined cDNA sequence for JP8A4
 25 SEQ ID NO: 285 is the determined cDNA sequence for JP8C3
 SEQ ID NO: 286 is the determined cDNA sequence for JP8G4
 SEQ ID NO: 287 is the determined cDNA sequence for JP8B6
 SEQ ID NO: 288 is the determined cDNA sequence for JP8D6
 SEQ ID NO: 289 is the determined cDNA sequence for JP8F5

SEQ ID NO: 290 is the determined cDNA sequence for JP8A8
 SEQ ID NO: 291 is the determined cDNA sequence for JP8C7
 SEQ ID NO: 292 is the determined cDNA sequence for JP8D7
 SEQ ID NO: 293 is the determined cDNA sequence for P8D8
 5 SEQ ID NO: 294 is the determined cDNA sequence for JP8E7
 SEQ ID NO: 295 is the determined cDNA sequence for JP8F8
 SEQ ID NO: 296 is the determined cDNA sequence for JP8G8
 SEQ ID NO: 297 is the determined cDNA sequence for JP8B10
 SEQ ID NO: 298 is the determined cDNA sequence for JP8C10
 10 SEQ ID NO: 299 is the determined cDNA sequence for JP8E9
 SEQ ID NO: 300 is the determined cDNA sequence for JP8E10
 SEQ ID NO: 301 is the determined cDNA sequence for JP8F9
 SEQ ID NO: 302 is the determined cDNA sequence for JP8H9
 SEQ ID NO: 303 is the determined cDNA sequence for JP8C12
 15 SEQ ID NO: 304 is the determined cDNA sequence for JP8E11
 SEQ ID NO: 305 is the determined cDNA sequence for JP8E12
 SEQ ID NO: 306 is the amino acid sequence for the peptide PS2#12
 SEQ ID NO: 307 is the determined cDNA sequence for P711P
 SEQ ID NO: 308 is the determined cDNA sequence for P712P
 20 SEQ ID NO: 309 is the determined cDNA sequence for CLONE23
 SEQ ID NO: 310 is the determined cDNA sequence for P774P
 SEQ ID NO: 311 is the determined cDNA sequence for P775P
 SEQ ID NO: 312 is the determined cDNA sequence for P715P
 SEQ ID NO: 313 is the determined cDNA sequence for P710P
 25 SEQ ID NO: 314 is the determined cDNA sequence for P767P
 SEQ ID NO: 315 is the determined cDNA sequence for P768P
 SEQ ID NO: 316-325 are the determined cDNA sequences of previously
 isolated genes
 SEQ ID NO: 326 is the determined cDNA sequence for P703PDE5

- SEQ ID NO: 327 is the predicted amino acid sequence for P703PDE5
- SEQ ID NO: 328 is the determined cDNA sequence for P703P6.26
- SEQ ID NO: 329 is the predicted amino acid sequence for P703P6.26
- SEQ ID NO: 330 is the determined cDNA sequence for P703PX-23
- 5 SEQ ID NO: 331 is the predicted amino acid sequence for P703PX-23
- SEQ ID NO: 332 is the determined full length cDNA sequence for P509S
- SEQ ID NO: 333 is the determined extended cDNA sequence for P707P
(also referred to as 11-C9)
- SEQ ID NO: 334 is the determined cDNA sequence for P714P
- 10 SEQ ID NO: 335 is the determined cDNA sequence for P705P (also
referred to as 9-F3)
- SEQ ID NO: 336 is the predicted amino acid sequence for P705P
- SEQ ID NO: 337 is the amino acid sequence of the peptide P1S#10
- SEQ ID NO: 338 is the amino acid sequence of the peptide p5
- 15 SEQ ID NO: 339 is the predicted amino acid sequence of P509S
- SEQ ID NO: 340 is the determined cDNA sequence for P778P
- SEQ ID NO: 341 is the determined cDNA sequence for P786P
- SEQ ID NO: 342 is the determined cDNA sequence for P789P
- SEQ ID NO: 343 is the determined cDNA sequence for a clone showing
20 homology to Homo sapiens MM46 mRNA
- SEQ ID NO: 344 is the determined cDNA sequence for a clone showing
homology to Homo sapiens TNF-alpha stimulated ABC protein (ABC50) mRNA
- SEQ ID NO: 345 is the determined cDNA sequence for a clone showing
homology to Homo sapiens mRNA for E-cadherin
- 25 SEQ ID NO: 346 is the determined cDNA sequence for a clone showing
homology to Human nuclear-encoded mitochondrial serine hydroxymethyltransferase
(SHMT)
- SEQ ID NO: 347 is the determined cDNA sequence for a clone showing
homology to Homo sapiens natural resistance-associated macrophage protein2 (NRAMP2)

SEQ ID NO: 348 is the determined cDNA sequence for a clone showing homology to Homo sapiens phosphoglucomutase-related protein (PGMRP)

SEQ ID NO: 349 is the determined cDNA sequence for a clone showing homology to Human mRNA for proteosome subunit p40

5 SEQ ID NO: 350 is the determined cDNA sequence for P777P

SEQ ID NO: 351 is the determined cDNA sequence for P779P

SEQ ID NO: 352 is the determined cDNA sequence for P790P

SEQ ID NO: 353 is the determined cDNA sequence for P784P

SEQ ID NO: 354 is the determined cDNA sequence for P776P

10 SEQ ID NO: 355 is the determined cDNA sequence for P780P

SEQ ID NO: 356 is the determined cDNA sequence for P544S

SEQ ID NO: 357 is the determined cDNA sequence for P745S

SEQ ID NO: 358 is the determined cDNA sequence for P782P

SEQ ID NO: 359 is the determined cDNA sequence for P783P

15 SEQ ID NO: 360 is the determined cDNA sequence for unknown 17984

SEQ ID NO: 361 is the determined cDNA sequence for P787P

SEQ ID NO: 362 is the determined cDNA sequence for P788P

SEQ ID NO: 363 is the determined cDNA sequence for unknown 17994

SEQ ID NO: 364 is the determined cDNA sequence for P781P

20 SEQ ID NO: 365 is the determined cDNA sequence for P785P

SEQ ID NO: 366-375 are the determined cDNA sequences for splice variants of B305D.

SEQ ID NO: 376 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 366.

25 SEQ ID NO: 377 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 372.

SEQ ID NO: 378 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 373.

SEQ ID NO: 379 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 374.

SEQ ID NO: 380 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 375.

- 5 SEQ ID NO: 381 is the determined cDNA sequence for B716P.
 SEQ ID NO: 382 is the determined full-length cDNA sequence for P711P.
 SEQ ID NO: 383 is the predicted amino acid sequence for P711P.
 SEQ ID NO: 384 is the cDNA sequence for P1000C.
 SEQ ID NO: 385 is the cDNA sequence for CGI-82.
- 10 SEQ ID NO:386 is the cDNA sequence for 23320.
 SEQ ID NO:387 is the cDNA sequence for CGI-69.
 SEQ ID NO:388 is the cDNA sequence for L-iditol-2-dehydrogenase.
 SEQ ID NO:389 is the cDNA sequence for 23379.
 SEQ ID NO:390 is the cDNA sequence for 23381.
- 15 SEQ ID NO:391 is the cDNA sequence for KIAA0122.
 SEQ ID NO:392 is the cDNA sequence for 23399.
 SEQ ID NO:393 is the cDNA sequence for a previously identified gene.
 SEQ ID NO:394 is the cDNA sequence for HCLBP.
 SEQ ID NO:395 is the cDNA sequence for transglutaminase.
- 20 SEQ ID NO:396 is the cDNA sequence for a previously identified gene.
 SEQ ID NO:397 is the cDNA sequence for PAP.
 SEQ ID NO:398 is the cDNA sequence for Ets transcription factor PDEF.
 SEQ ID NO:399 is the cDNA sequence for hTGR.
 SEQ ID NO:400 is the cDNA sequence for KIAA0295.
- 25 SEQ ID NO:401 is the cDNA sequence for 22545.
 SEQ ID NO:402 is the cDNA sequence for 22547.
 SEQ ID NO:403 is the cDNA sequence for 22548.
 SEQ ID NO:404 is the cDNA sequence for 22550.
 SEQ ID NO:405 is the cDNA sequence for 22551.

SEQ ID NO:406 is the cDNA sequence for 22552.

SEQ ID NO:407 is the cDNA sequence for 22553 (also known as P1020C).

SEQ ID NO:408 is the cDNA sequence for 22558.

SEQ ID NO:409 is the cDNA sequence for 22562.

5 SEQ ID NO:410 is the cDNA sequence for 22565.

SEQ ID NO:411 is the cDNA sequence for 22567.

SEQ ID NO:412 is the cDNA sequence for 22568.

SEQ ID NO:413 is the cDNA sequence for 22570.

SEQ ID NO:414 is the cDNA sequence for 22571.

10 SEQ ID NO:415 is the cDNA sequence for 22572.

SEQ ID NO:416 is the cDNA sequence for 22573.

SEQ ID NO:417 is the cDNA sequence for 22573.

SEQ ID NO:418 is the cDNA sequence for 22575.

SEQ ID NO:419 is the cDNA sequence for 22580.

15 SEQ ID NO:420 is the cDNA sequence for 22581.

SEQ ID NO:421 is the cDNA sequence for 22582.

SEQ ID NO:422 is the cDNA sequence for 22583.

SEQ ID NO:423 is the cDNA sequence for 22584.

SEQ ID NO:424 is the cDNA sequence for 22585.

20 SEQ ID NO:425 is the cDNA sequence for 22586.

SEQ ID NO:426 is the cDNA sequence for 22587.

SEQ ID NO:427 is the cDNA sequence for 22588.

SEQ ID NO:428 is the cDNA sequence for 22589.

SEQ ID NO:429 is the cDNA sequence for 22590.

25 SEQ ID NO:430 is the cDNA sequence for 22591.

SEQ ID NO:431 is the cDNA sequence for 22592.

SEQ ID NO:432 is the cDNA sequence for 22593.

SEQ ID NO:433 is the cDNA sequence for 22594.

SEQ ID NO:434 is the cDNA sequence for 22595.

SEQ ID NO:435 is the cDNA sequence for 22596.
 SEQ ID NO:436 is the cDNA sequence for 22847.
 SEQ ID NO:437 is the cDNA sequence for 22848.
 SEQ ID NO:438 is the cDNA sequence for 22849.
 5 SEQ ID NO:439 is the cDNA sequence for 22851.
 SEQ ID NO:440 is the cDNA sequence for 22852.
 SEQ ID NO:441 is the cDNA sequence for 22853.
 SEQ ID NO:442 is the cDNA sequence for 22854.
 SEQ ID NO:443 is the cDNA sequence for 22855.
 10 SEQ ID NO:444 is the cDNA sequence for 22856.
 SEQ ID NO:445 is the cDNA sequence for 22857.
 SEQ ID NO:446 is the cDNA sequence for 23601.
 SEQ ID NO:447 is the cDNA sequence for 23602.
 SEQ ID NO:448 is the cDNA sequence for 23605.
 15 SEQ ID NO:449 is the cDNA sequence for 23606.
 SEQ ID NO:450 is the cDNA sequence for 23612.
 SEQ ID NO:451 is the cDNA sequence for 23614.
 SEQ ID NO:452 is the cDNA sequence for 23618.
 SEQ ID NO:453 is the cDNA sequence for 23622.
 20 SEQ ID NO:454 is the cDNA sequence for folate hydrolase.
 SEQ ID NO:455 is the cDNA sequence for LIM protein.
 SEQ ID NO:456 is the cDNA sequence for a known gene.
 SEQ ID NO:457 is the cDNA sequence for a known gene.
 SEQ ID NO:458 is the cDNA sequence for a previously identified gene.
 25 SEQ ID NO:459 is the cDNA sequence for 23045.
 SEQ ID NO:460 is the cDNA sequence for 23032.
 SEQ ID NO:461 is the cDNA sequence for 23054.
 SEQ ID NO:462-467 are cDNA sequences for known genes.
 SEQ ID NO:468-471 are cDNA sequences for P710P.

SEQ ID NO:472 is a cDNA sequence for P1001C.

SEQ ID NO: 473 is the determined cDNA sequence for a first splice variant of P775P (referred to as 27505).

5 SEQ ID NO: 474 is the determined cDNA sequence for a second splice variant of P775P (referred to as 19947).

SEQ ID NO: 475 is the determined cDNA sequence for a third splice variant of P775P (referred to as 19941).

SEQ ID NO: 476 is the determined cDNA sequence for a fourth splice variant of P775P (referred to as 19937).

10 SEQ ID NO: 477 is a first predicted amino acid sequence encoded by the sequence of SEQ ID NO: 474.

SEQ ID NO: 478 is a second predicted amino acid sequence encoded by the sequence of SEQ ID NO: 474.

15 SEQ ID NO: 479 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 475.

SEQ ID NO: 480 is a first predicted amino acid sequence encoded by the sequence of SEQ ID NO: 473.

SEQ ID NO: 481 is a second predicted amino acid sequence encoded by the sequence of SEQ ID NO: 473.

20 SEQ ID NO: 482 is a third predicted amino acid sequence encoded by the sequence of SEQ ID NO: 473.

SEQ ID NO: 483 is a fourth predicted amino acid sequence encoded by the sequence of SEQ ID NO: 473.

25 SEQ ID NO: 484 is the first 30 amino acids of the *M. tuberculosis* antigen Ra12.

SEQ ID NO: 485 is the PCR primer AW025.

SEQ ID NO: 486 is the PCR primer AW003.

SEQ ID NO: 487 is the PCR primer AW027.

SEQ ID NO: 488 is the PCR primer AW026.

SEQ ID NO: 489-501 are peptides employed in epitope mapping studies.

SEQ ID NO: 502 is the determined cDNA sequence of the complementarity determining region for the anti-P503S monoclonal antibody 20D4.

5 SEQ ID NO: 503 is the determined cDNA sequence of the complementarity determining region for the anti-P503S monoclonal antibody JA1.

SEQ ID NO: 504 & 505 are peptides employed in epitope mapping studies.

SEQ ID NO: 506 is the determined cDNA sequence of the complementarity determining region for the anti-P703P monoclonal antibody 8H2.

10 SEQ ID NO: 507 is the determined cDNA sequence of the complementarity determining region for the anti-P703P monoclonal antibody 7H8.

SEQ ID NO: 508 is the determined cDNA sequence of the complementarity determining region for the anti-P703P monoclonal antibody 2D4.

SEQ ID NO: 509-522 are peptides employed in epitope mapping studies.

15 SEQ ID NO: 523 is a mature form of P703P used to raise antibodies against P703P.

SEQ ID NO: 524 is the putative full-length cDNA sequence of P703P.

SEQ ID NO: 525 is the predicted amino acid sequence encoded by SEQ ID NO: 524.

SEQ ID NO: 526 is the full-length cDNA sequence for P790P.

20 SEQ ID NO: 527 is the predicted amino acid sequence for P790P.

SEQ ID NO: 528 & 529 are PCR primers.

SEQ ID NO: 530 is the cDNA sequence of a splice variant of SEQ ID NO: 366.

25 SEQ ID NO: 531 is the cDNA sequence of the open reading frame of SEQ ID NO: 530.

SEQ ID NO: 532 is the predicted amino acid encoded by the sequence of SEQ ID NO: 531.

SEQ ID NO: 533 is the DNA sequence of a putative ORF of P775P.

SEQ ID NO: 534 is the predicted amino acid sequence encoded by SEQ ID NO: 533.

SEQ ID NO: 535 is a first full-length cDNA sequence for P510S.

SEQ ID NO: 536 is a second full-length cDNA sequence for P510S.

5 SEQ ID NO: 537 is the predicted amino acid sequence encoded by SEQ ID NO: 535.

SEQ ID NO: 538 is the predicted amino acid sequence encoded by SEQ ID NO: 536.

SEQ ID NO: 539 is the peptide P501S-370.

10 SEQ ID NO: 540 is the peptide P501S-376.

SEQ ID NO: 541-551 are epitopes of P501S.

SEQ ID NO: 552 is an extended cDNA sequence for P712P.

SEQ ID NO: 553-568 are the amino acid sequences encoded by predicted open reading frames within SEQ ID NO: 552.

15 SEQ ID NO: 569 is an extended cDNA sequence for P776P.

SEQ ID NO: 570 is the determined cDNA sequence for a splice variant of P776P referred to as contig 6.

SEQ ID NO: 571 is the determined cDNA sequence for a splice variant of P776P referred to as contig 7.

20 SEQ ID NO: 572 is the determined cDNA sequence for a splice variant of P776P referred to as contig 14.

SEQ ID NO: 573 is the amino acid sequence encoded by a first predicted ORF of SEQ ID NO: 570.

25 SEQ ID NO: 574 is the amino acid sequence encoded by a second predicted ORF of SEQ ID NO: 570.

SEQ ID NO: 575 is the amino acid sequence encoded by a predicted ORF of SEQ ID NO: 571.

SEQ ID NO: 576-586 are amino acid sequences encoded by predicted ORFs of SEQ ID NO: 569.

SEQ ID NO: 587 is a DNA consensus sequence of the sequences of P767P and P777P.

SEQ ID NO: 588-590 are amino acid sequences encoded by predicted ORFs of SEQ ID NO: 587.

5 SEQ ID NO: 591 is an extended cDNA sequence for P1020C.

SEQ ID NO: 592 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: P1020C.

SEQ ID NO: 593 is a splice variant of P775P referred to as 50748.

10 SEQ ID NO: 594 is a splice variant of P775P referred to as 50717. SEQ ID NO: 595 is a splice variant of P775P referred to as 45985.

SEQ ID NO: 596 is a splice variant of P775P referred to as 38769.

SEQ ID NO: 597 is a splice variant of P775P referred to as 37922.

SEQ ID NO: 598 is a splice variant of P510S referred to as 49274.

SEQ ID NO: 599 is a splice variant of P510S referred to as 39487.

15 SEQ ID NO: 600 is a splice variant of P504S referred to as 5167.16.

SEQ ID NO: 601 is a splice variant of P504S referred to as 5167.1.

SEQ ID NO: 602 is a splice variant of P504S referred to as 5163.46.

SEQ ID NO: 603 is a splice variant of P504S referred to as 5163.42.

SEQ ID NO: 604 is a splice variant of P504S referred to as 5163.34.

20 SEQ ID NO: 605 is a splice variant of P504S referred to as 5163.17.

SEQ ID NO: 606 is a splice variant of P501S referred to as 10640.

SEQ ID NO: 607-615 are the sequences of PCR primers.

SEQ ID NO: 616 is the determined cDNA sequence of a fusion of P703P and PSA.

25 SEQ ID NO: 617 is the amino acid sequence of the fusion of P703P and PSA.

SEQ ID NO: 618-689 are determined cDNA sequences of prostate-specific clones.

SEQ ID NO: 690 is the cDNA sequence of the gene DD3.

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SEQ ID NO: 779 is the determined cDNA sequence for a polymorphic variant of P788P.

- SEQ ID NO: 780 is the amino acid sequence encoded by SEQ ID NO: 779.
- SEQ ID NO: 781 is the amino acid sequence of peptide 4 from P703P.
- SEQ ID NO: 782 is the cDNA sequence that encodes peptide 4 from P703P.
- SEQ ID NO: 783-798 are the cDNA sequence encoding epitopes of P703P.
- 5 SEQ ID NO: 799-814 are the amino acid sequences of epitopes of P703P.
- SEQ ID NO: 815 and 816 are PCR primers.
- SEQ ID NO: 817 is the cDNA sequence encoding an N-terminal portion of P788P expressed in *E. coli*.
- 10 SEQ ID NO: 818 is the amino acid sequence of the N-terminal portion of P788P expressed in *E. coli*.
- SEQ ID NO: 819 is the amino acid sequence of the *M. tuberculosis* antigen Ra12.
- SEQ ID NO: 820 and 821 are PCR primers.
- SEQ ID NO: 822 is the cDNA sequence for the Ra12-P510S-C construct.
- 15 SEQ ID NO: 823 is the cDNA sequence for the P510S-C construct.
- SEQ ID NO: 824 is the cDNA sequence for the P510S-E3 construct.
- SEQ ID NO: 825 is the amino acid sequence for the Ra12-P510S-C construct.
- SEQ ID NO: 826 is the amino acid sequence for the P510S-C construct.
- 20 SEQ ID NO: 827 is the amino acid sequence for the P510S-E3 construct.
- SEQ ID NO: 828-833 are PCR primers.
- SEQ ID NO: 834 is the cDNA sequence of the construct Ra12-P775P-ORF3.
- 25 SEQ ID NO: 835 is the amino acid sequence of the construct Ra12-P775P-ORF3.
- SEQ ID NO: 836 and 837 are PCR primers.
- SEQ ID NO: 838 is the determined amino acid sequence for a P703P His tag fusion protein.

SEQ ID NO: 839 is the determined cDNA sequence for a P703P His tag fusion protein.

SEQ ID NO: 840 and 841 are PCR primers.

5 fusion protein. SEQ ID NO: 842 is the determined amino acid sequence for a P705P His tag fusion protein.

SEQ ID NO: 843 is the determined cDNA sequence for a P705P His tag fusion protein.

SEQ ID NO: 844 and 845 are PCR primers.

10 fusion protein. SEQ ID NO: 846 is the determined amino acid sequence for a P711P His tag fusion protein.

SEQ ID NO: 847 is the determined cDNA sequence for a P711P His tag fusion protein.

SEQ ID NO: 848 is the amino acid sequence of the *M. tuberculosis* antigen Ra12.

15 SEQ ID NO: 849 and 850 are PCR primers.

SEQ ID NO: 851 is the determined cDNA sequence for the construct Ra12-P501S-E2.

SEQ ID NO: 852 is the determined amino acid sequence for the construct Ra12-P501S-E2.

20 SEQ ID NO: 853 is the amino acid sequence for an epitope of P501S.

SEQ ID NO: 854 is the DNA sequence encoding SEQ ID NO: 853.

SEQ ID NO: 855 is the amino acid sequence for an epitope of P501S.

SEQ ID NO: 856 is the DNA sequence encoding SEQ ID NO: 855.

SEQ ID NO: 857 is a peptide employed in epitope mapping studies.

25 SEQ ID NO: 858 is the amino acid sequence for an epitope of P501S.

SEQ ID NO: 859 is the DNA sequence encoding SEQ ID NO: 858.

SEQ ID NO: 860-862 are the amino acid sequences for CD4 epitopes of P501S.

SEQ ID NO: 863-865 are the DNA sequences encoding the sequences of
SEQ ID NO: 860-862.

DETAILED DESCRIPTION OF THE INVENTION

5 As noted above, the present invention is generally directed to compositions
and methods for using the compositions, for example in the therapy and diagnosis of
cancer, such as prostate cancer. Certain illustrative compositions described herein include
prostate-specific polypeptides, polynucleotides encoding such polypeptides, binding agents
such as antibodies, antigen presenting cells (APCs) and/or immune system cells (*e.g.*, T
10 cells). A "prostate-specific protein," as the term is used herein, refers generally to a protein
that is expressed in prostate cells at a level that is at least two fold, and preferably at least
five fold, greater than the level of expression in other normal tissues, as determined using a
representative assay provided herein. Certain prostate-specific proteins are tumor proteins
that react detectably (within an immunoassay, such as an ELISA or Western blot) with
15 antisera of a patient afflicted with prostate cancer.

Therefore, in accordance with the above, and as described further below, the
present invention provides illustrative polynucleotide compositions having sequences set
forth in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-
335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587,
20 591, 593-606, 618-705, 709-774, 777, 789, 817, 823 and 824, illustrative polypeptide
compositions having amino acid sequences set forth in SEQ ID NO: 112-114, 172, 176,
178, 327, 329, 331, 336, 339, 376-380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525,
527, 532, 534, 537-551, 553-568, 573-586, 588-590, 592, 706-708, 775, 776, 778, 780,
781, 811, 814, 818, 826, 827, 853, 855, 858 and 860-862, antibody compositions capable
25 of binding such polypeptides, and numerous additional embodiments employing such
compositions, for example in the detection, diagnosis and/or therapy of human prostate
cancer.

POLYNUCLEOTIDE COMPOSITIONS

As used herein, the terms "DNA segment" and "polynucleotide" refer to a DNA molecule that has been isolated free of total genomic DNA of a particular species. Therefore, a DNA segment encoding a polypeptide refers to a DNA segment that contains one or more coding sequences yet is substantially isolated away from, or purified free from, total genomic DNA of the species from which the DNA segment is obtained. Included within the terms "DNA segment" and "polynucleotide" are DNA segments and smaller fragments of such segments, and also recombinant vectors, including, for example, plasmids, cosmids, phagemids, phage, viruses, and the like.

As will be understood by those skilled in the art, the DNA segments of this invention can include genomic sequences, extra-genomic and plasmid-encoded sequences and smaller engineered gene segments that express, or may be adapted to express, proteins, polypeptides, peptides and the like. Such segments may be naturally isolated, or modified synthetically by the hand of man.

"Isolated," as used herein, means that a polynucleotide is substantially away from other coding sequences, and that the DNA segment does not contain large portions of unrelated coding DNA, such as large chromosomal fragments or other functional genes or polypeptide coding regions. Of course, this refers to the DNA segment as originally isolated, and does not exclude genes or coding regions later added to the segment by the hand of man.

As will be recognized by the skilled artisan, polynucleotides may be single-stranded (coding or antisense) or double-stranded, and may be DNA (genomic, cDNA or synthetic) or RNA molecules. RNA molecules include HnRNA molecules, which contain introns and correspond to a DNA molecule in a one-to-one manner, and mRNA molecules, which do not contain introns. Additional coding or non-coding sequences may, but need not, be present within a polynucleotide of the present invention, and a polynucleotide may, but need not, be linked to other molecules and/or support materials.

Polynucleotides may comprise a native sequence (*i.e.*, an endogenous sequence that encodes a prostate-specific protein or a portion thereof) or may comprise a

variant, or a biological or antigenic functional equivalent of such a sequence. Polynucleotide variants may contain one or more substitutions, additions, deletions and/or insertions, as further described below, preferably such that the immunogenicity of the encoded polypeptide is not diminished, relative to a native tumor protein. The effect on the
 5 immunogenicity of the encoded polypeptide may generally be assessed as described herein. The term “variants” also encompasses homologous genes of xenogenic origin.

When comparing polynucleotide or polypeptide sequences, two sequences are said to be “identical” if the sequence of nucleotides or amino acids in the two sequences is the same when aligned for maximum correspondence, as described below. Comparisons
 10 between two sequences are typically performed by comparing the sequences over a comparison window to identify and compare local regions of sequence similarity. A “comparison window” as used herein, refers to a segment of at least about 20 contiguous positions, usually 30 to about 75, 40 to about 50, in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences
 15 are optimally aligned.

Optimal alignment of sequences for comparison may be conducted using the Megalign program in the Lasergene suite of bioinformatics software (DNASTAR, Inc., Madison, WI), using default parameters. This program embodies several alignment schemes described in the following references: Dayhoff, M.O. (1978) A model of
 20 evolutionary change in proteins – Matrices for detecting distant relationships. In Dayhoff, M.O. (ed.) Atlas of Protein Sequence and Structure, National Biomedical Research Foundation, Washington DC Vol. 5, Suppl. 3, pp. 345-358; Hein J. (1990) Unified Approach to Alignment and Phylogenesis pp. 626-645 *Methods in Enzymology* vol. 183, Academic Press, Inc., San Diego, CA; Higgins, D.G. and Sharp, P.M. (1989) *CABIOS*
 25 5:151-153; Myers, E.W. and Muller W. (1988) *CABIOS* 4:11-17; Robinson, E.D. (1971) *Comb. Theor* 11:105; Santou, N. Nes, M. (1987) *Mol. Biol. Evol.* 4:406-425; Sneath, P.H.A. and Sokal, R.R. (1973) *Numerical Taxonomy – the Principles and Practice of Numerical Taxonomy*, Freeman Press, San Francisco, CA; Wilbur, W.J. and Lipman, D.J. (1983) *Proc. Natl. Acad., Sci. USA* 80:726-730.

Alternatively, optimal alignment of sequences for comparison may be conducted by the local identity algorithm of Smith and Waterman (1981) *Add. APL. Math* 2:482, by the identity alignment algorithm of Needleman and Wunsch (1970) *J. Mol. Biol.* 48:443, by the search for similarity methods of Pearson and Lipman (1988) *Proc. Natl. Acad. Sci. USA* 85: 2444, by computerized implementations of these algorithms (GAP, BESTFIT, BLAST, FASTA, and TFASTA in the Wisconsin Genetics Software Package, Genetics Computer Group (GCG), 575 Science Dr., Madison, WI), or by inspection.

One preferred example of algorithms that are suitable for determining percent sequence identity and sequence similarity are the BLAST and BLAST 2.0 algorithms, which are described in Altschul *et al.* (1977) *Nucl. Acids Res.* 25:3389-3402 and Altschul *et al.* (1990) *J. Mol. Biol.* 215:403-410, respectively. BLAST and BLAST 2.0 can be used, for example with the parameters described herein, to determine percent sequence identity for the polynucleotides and polypeptides of the invention. Software for performing BLAST analyses is publicly available through the National Center for Biotechnology Information. In one illustrative example, cumulative scores can be calculated using, for nucleotide sequences, the parameters M (reward score for a pair of matching residues; always >0) and N (penalty score for mismatching residues; always <0). For amino acid sequences, a scoring matrix can be used to calculate the cumulative score. Extension of the word hits in each direction are halted when: the cumulative alignment score falls off by the quantity X from its maximum achieved value; the cumulative score goes to zero or below, due to the accumulation of one or more negative-scoring residue alignments; or the end of either sequence is reached. The BLAST algorithm parameters W, T and X determine the sensitivity and speed of the alignment. The BLASTN program (for nucleotide sequences) uses as defaults a wordlength (W) of 11, and expectation (E) of 10, and the BLOSUM62 scoring matrix (see Henikoff and Henikoff (1989) *Proc. Natl. Acad. Sci. USA* 89:10915) alignments, (B) of 50, expectation (E) of 10, M=5, N=-4 and a comparison of both strands.

Preferably, the "percentage of sequence identity" is determined by comparing two optimally aligned sequences over a window of comparison of at least 20

positions, wherein the portion of the polynucleotide or polypeptide sequence in the comparison window may comprise additions or deletions (*i.e.*, gaps) of 20 percent or less, usually 5 to 15 percent, or 10 to 12 percent, as compared to the reference sequences (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage is calculated by determining the number of positions at which the identical nucleic acid bases or amino acid residue occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the reference sequence (*i.e.*, the window size) and multiplying the results by 100 to yield the percentage of sequence identity.

Therefore, the present invention encompasses polynucleotide and polypeptide sequences having substantial identity to the sequences disclosed herein, for example those comprising at least 50% sequence identity, preferably at least 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% or higher, sequence identity compared to a polynucleotide or polypeptide sequence of this invention using the methods described herein, (*e.g.*, BLAST analysis using standard parameters, as described below). One skilled in this art will recognize that these values can be appropriately adjusted to determine corresponding identity of proteins encoded by two nucleotide sequences by taking into account codon degeneracy, amino acid similarity, reading frame positioning and the like.

In additional embodiments, the present invention provides isolated polynucleotides and polypeptides comprising various lengths of contiguous stretches of sequence identical to or complementary to one or more of the sequences disclosed herein. For example, polynucleotides are provided by this invention that comprise at least about 15, 20, 30, 40, 50, 75, 100, 150, 200, 300, 400, 500 or 1000 or more contiguous nucleotides of one or more of the sequences disclosed herein as well as all intermediate lengths there between. It will be readily understood that "intermediate lengths", in this context, means any length between the quoted values, such as 16, 17, 18, 19, *etc.*; 21, 22, 23, *etc.*; 30, 31, 32, *etc.*; 50, 51, 52, 53, *etc.*; 100, 101, 102, 103, *etc.*; 150, 151, 152, 153, *etc.*; including all integers through 200-500; 500-1,000, and the like.

The polynucleotides of the present invention, or fragments thereof, regardless of the length of the coding sequence itself, may be combined with other DNA sequences, such as promoters, polyadenylation signals, additional restriction enzyme sites, multiple cloning sites, other coding segments, and the like, such that their overall length
 5 may vary considerably. It is therefore contemplated that a nucleic acid fragment of almost any length may be employed, with the total length preferably being limited by the ease of preparation and use in the intended recombinant DNA protocol. For example, illustrative DNA segments with total lengths of about 10,000, about 5000, about 3000, about 2,000, about 1,000, about 500, about 200, about 100, about 50 base pairs in length, and the like,
 10 (including all intermediate lengths) are contemplated to be useful in many implementations of this invention.

In other embodiments, the present invention is directed to polynucleotides that are capable of hybridizing under moderately stringent conditions to a polynucleotide sequence provided herein, or a fragment thereof, or a complementary sequence thereof.
 15 Hybridization techniques are well known in the art of molecular biology. For purposes of illustration, suitable moderately stringent conditions for testing the hybridization of a polynucleotide of this invention with other polynucleotides include prewashing in a solution of 5 X SSC, 0.5% SDS, 1.0 mM EDTA (pH 8.0); hybridizing at 50°C-65°C, 5 X SSC, overnight; followed by washing twice at 65°C for 20 minutes with each of 2X, 0.5X
 20 and 0.2X SSC containing 0.1% SDS.

Moreover, it will be appreciated by those of ordinary skill in the art that, as a result of the degeneracy of the genetic code, there are many nucleotide sequences that encode a polypeptide as described herein. Some of these polynucleotides bear minimal homology to the nucleotide sequence of any native gene. Nonetheless, polynucleotides that
 25 vary due to differences in codon usage are specifically contemplated by the present invention. Further, alleles of the genes comprising the polynucleotide sequences provided herein are within the scope of the present invention. Alleles are endogenous genes that are altered as a result of one or more mutations, such as deletions, additions and/or substitutions of nucleotides. The resulting mRNA and protein may, but need not, have an

altered structure or function. Alleles may be identified using standard techniques (such as hybridization, amplification and/or database sequence comparison).

PROBES AND PRIMERS

In other embodiments of the present invention, the polynucleotide sequences provided herein can be advantageously used as probes or primers for nucleic acid hybridization. As such, it is contemplated that nucleic acid segments that comprise a sequence region of at least about 15 nucleotide long contiguous sequence that has the same sequence as, or is complementary to, a 15 nucleotide long contiguous sequence disclosed herein will find particular utility. Longer contiguous identical or complementary sequences, *e.g.*, those of about 20, 30, 40, 50, 100, 200, 500, 1000 (including all intermediate lengths) and even up to full length sequences will also be of use in certain embodiments.

The ability of such nucleic acid probes to specifically hybridize to a sequence of interest will enable them to be of use in detecting the presence of complementary sequences in a given sample. However, other uses are also envisioned, such as the use of the sequence information for the preparation of mutant species primers, or primers for use in preparing other genetic constructions.

Polynucleotide molecules having sequence regions consisting of contiguous nucleotide stretches of 10-14, 15-20, 30, 50, or even of 100-200 nucleotides or so (including intermediate lengths as well), identical or complementary to a polynucleotide sequence disclosed herein, are particularly contemplated as hybridization probes for use in, *e.g.*, Southern and Northern blotting. This would allow a gene product, or fragment thereof, to be analyzed, both in diverse cell types and also in various bacterial cells. The total size of fragment, as well as the size of the complementary stretch(es), will ultimately depend on the intended use or application of the particular nucleic acid segment. Smaller fragments will generally find use in hybridization embodiments, wherein the length of the contiguous complementary region may be varied, such as between about 15 and about 100

nucleotides, but larger contiguous complementarity stretches may be used, according to the length complementary sequences one wishes to detect.

The use of a hybridization probe of about 15-25 nucleotides in length allows the formation of a duplex molecule that is both stable and selective. Molecules having
 5 contiguous complementary sequences over stretches greater than 15 bases in length are generally preferred, though, in order to increase stability and selectivity of the hybrid, and thereby improve the quality and degree of specific hybrid molecules obtained. One will generally prefer to design nucleic acid molecules having gene-complementary stretches of 15 to 25 contiguous nucleotides, or even longer where desired.

10 Hybridization probes may be selected from any portion of any of the sequences disclosed herein. All that is required is to review the sequence set forth in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823 and 824, or to any continuous portion of
 15 the sequence, from about 15-25 nucleotides in length up to and including the full length sequence, that one wishes to utilize as a probe or primer. The choice of probe and primer sequences may be governed by various factors. For example, one may wish to employ primers from towards the termini of the total sequence.

Small polynucleotide segments or fragments may be readily prepared by, for
 20 example, directly synthesizing the fragment by chemical means, as is commonly practiced using an automated oligonucleotide synthesizer. Also, fragments may be obtained by application of nucleic acid reproduction technology, such as the PCR™ technology of U. S. Patent 4,683,202 (incorporated herein by reference), by introducing selected sequences into recombinant vectors for recombinant production, and by other recombinant DNA
 25 techniques generally known to those of skill in the art of molecular biology.

The nucleotide sequences of the invention may be used for their ability to selectively form duplex molecules with complementary stretches of the entire gene or gene fragments of interest. Depending on the application envisioned, one will typically desire to employ varying conditions of hybridization to achieve varying degrees of selectivity of

probe towards target sequence. For applications requiring high selectivity, one will typically desire to employ relatively stringent conditions to form the hybrids, *e.g.*, one will select relatively low salt and/or high temperature conditions, such as provided by a salt concentration of from about 0.02 M to about 0.15 M salt at temperatures of from about
 5 50°C to about 70°C. Such selective conditions tolerate little, if any, mismatch between the probe and the template or target strand, and would be particularly suitable for isolating related sequences.

Of course, for some applications, for example, where one desires to prepare mutants employing a mutant primer strand hybridized to an underlying template, less
 10 stringent (reduced stringency) hybridization conditions will typically be needed in order to allow formation of the heteroduplex. In these circumstances, one may desire to employ salt conditions such as those of from about 0.15 M to about 0.9 M salt, at temperatures ranging from about 20°C to about 55°C. Cross-hybridizing species can thereby be readily identified as positively hybridizing signals with respect to control hybridizations. In any
 15 case, it is generally appreciated that conditions can be rendered more stringent by the addition of increasing amounts of formamide, which serves to destabilize the hybrid duplex in the same manner as increased temperature. Thus, hybridization conditions can be readily manipulated, and thus will generally be a method of choice depending on the desired results.

20 POLYNUCLEOTIDE IDENTIFICATION AND CHARACTERIZATION

Polynucleotides may be identified, prepared and/or manipulated using any of a variety of well established techniques. For example, a polynucleotide may be identified, as described in more detail below, by screening a microarray of cDNAs for tumor-associated expression (*i.e.*, expression that is at least two fold greater in a tumor than
 25 in normal tissue, as determined using a representative assay provided herein). Such screens may be performed, for example, using a Synteni microarray (Palo Alto, CA) according to the manufacturer's instructions (and essentially as described by Schena *et al.*, *Proc. Natl. Acad. Sci. USA* 93:10614-10619, 1996 and Heller *et al.*, *Proc. Natl. Acad. Sci. USA*

94:2150-2155, 1997). Alternatively, polynucleotides may be amplified from cDNA prepared from cells expressing the proteins described herein, such as prostate-specific cells. Such polynucleotides may be amplified via polymerase chain reaction (PCR). For this approach, sequence-specific primers may be designed based on the sequences provided
 5 herein, and may be purchased or synthesized.

An amplified portion of a polynucleotide of the present invention may be used to isolate a full length gene from a suitable library (*e.g.*, a prostate tumor cDNA library) using well known techniques. Within such techniques, a library (cDNA or genomic) is screened using one or more polynucleotide probes or primers suitable for
 10 amplification. Preferably, a library is size-selected to include larger molecules. Random primed libraries may also be preferred for identifying 5' and upstream regions of genes. Genomic libraries are preferred for obtaining introns and extending 5' sequences.

For hybridization techniques, a partial sequence may be labeled (*e.g.*, by nick-translation or end-labeling with ^{32}P) using well known techniques. A bacterial or
 15 bacteriophage library is then generally screened by hybridizing filters containing denatured bacterial colonies (or lawns containing phage plaques) with the labeled probe (*see* Sambrook *et al.*, *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY, 1989). Hybridizing colonies or plaques are selected and expanded, and the DNA is isolated for further analysis. cDNA clones may be
 20 analyzed to determine the amount of additional sequence by, for example, PCR using a primer from the partial sequence and a primer from the vector. Restriction maps and partial sequences may be generated to identify one or more overlapping clones. The complete sequence may then be determined using standard techniques, which may involve generating a series of deletion clones. The resulting overlapping sequences can then
 25 assembled into a single contiguous sequence. A full length cDNA molecule can be generated by ligating suitable fragments, using well known techniques.

Alternatively, there are numerous amplification techniques for obtaining a full length coding sequence from a partial cDNA sequence. Within such techniques, amplification is generally performed via PCR. Any of a variety of commercially available

kits may be used to perform the amplification step. Primers may be designed using, for example, software well known in the art. Primers are preferably 22-30 nucleotides in length, have a GC content of at least 50% and anneal to the target sequence at temperatures of about 68°C to 72°C. The amplified region may be sequenced as described above, and
 5 overlapping sequences assembled into a contiguous sequence.

One such amplification technique is inverse PCR (*see* Triglia *et al.*, *Nucl. Acids Res.* 16:8186, 1988), which uses restriction enzymes to generate a fragment in the known region of the gene. The fragment is then circularized by intramolecular ligation and used as a template for PCR with divergent primers derived from the known region. Within
 10 an alternative approach, sequences adjacent to a partial sequence may be retrieved by amplification with a primer to a linker sequence and a primer specific to a known region. The amplified sequences are typically subjected to a second round of amplification with the same linker primer and a second primer specific to the known region. A variation on this procedure, which employs two primers that initiate extension in opposite directions from
 15 the known sequence, is described in WO 96/38591. Another such technique is known as "rapid amplification of cDNA ends" or RACE. This technique involves the use of an internal primer and an external primer, which hybridizes to a polyA region or vector sequence, to identify sequences that are 5' and 3' of a known sequence. Additional techniques include capture PCR (Lagerstrom *et al.*, *PCR Methods Applic.* 1:111-19, 1991)
 20 and walking PCR (Parker *et al.*, *Nucl. Acids. Res.* 19:3055-60, 1991). Other methods employing amplification may also be employed to obtain a full length cDNA sequence.

In certain instances, it is possible to obtain a full length cDNA sequence by analysis of sequences provided in an expressed sequence tag (EST) database, such as that available from GenBank. Searches for overlapping ESTs may generally be performed
 25 using well known programs (*e.g.*, NCBI BLAST searches), and such ESTs may be used to generate a contiguous full length sequence. Full length DNA sequences may also be obtained by analysis of genomic fragments.

POLYNUCLEOTIDE EXPRESSION IN HOST CELLS

In other embodiments of the invention, polynucleotide sequences or fragments thereof which encode polypeptides of the invention, or fusion proteins or functional equivalents thereof, may be used in recombinant DNA molecules to direct
5 expression of a polypeptide in appropriate host cells. Due to the inherent degeneracy of the genetic code, other DNA sequences that encode substantially the same or a functionally equivalent amino acid sequence may be produced and these sequences may be used to clone and express a given polypeptide.

As will be understood by those of skill in the art, it may be advantageous in
10 some instances to produce polypeptide-encoding nucleotide sequences possessing non-naturally occurring codons. For example, codons preferred by a particular prokaryotic or eukaryotic host can be selected to increase the rate of protein expression or to produce a recombinant RNA transcript having desirable properties, such as a half-life which is longer than that of a transcript generated from the naturally occurring sequence.

Moreover, the polynucleotide sequences of the present invention can be
15 engineered using methods generally known in the art in order to alter polypeptide encoding sequences for a variety of reasons, including but not limited to, alterations which modify the cloning, processing, and/or expression of the gene product. For example, DNA shuffling by random fragmentation and PCR reassembly of gene fragments and synthetic
20 oligonucleotides may be used to engineer the nucleotide sequences. In addition, site-directed mutagenesis may be used to insert new restriction sites, alter glycosylation patterns, change codon preference, produce splice variants, or introduce mutations, and so forth.

In another embodiment of the invention, natural, modified, or recombinant
25 nucleic acid sequences may be ligated to a heterologous sequence to encode a fusion protein. For example, to screen peptide libraries for inhibitors of polypeptide activity, it may be useful to encode a chimeric protein that can be recognized by a commercially available antibody. A fusion protein may also be engineered to contain a cleavage site

located between the polypeptide-encoding sequence and the heterologous protein sequence, so that the polypeptide may be cleaved and purified away from the heterologous moiety.

Sequences encoding a desired polypeptide may be synthesized, in whole or in part, using chemical methods well known in the art (see Caruthers, M. H. *et al.* (1980) *Nucl. Acids Res. Symp. Ser.* 215-223, Horn, T. *et al.* (1980) *Nucl. Acids Res. Symp. Ser.* 225-232). Alternatively, the protein itself may be produced using chemical methods to synthesize the amino acid sequence of a polypeptide, or a portion thereof. For example, peptide synthesis can be performed using various solid-phase techniques (Roberge, J. Y. *et al.* (1995) *Science* 269:202-204) and automated synthesis may be achieved, for example, using the ABI 431A Peptide Synthesizer (Perkin Elmer, Palo Alto, CA).

A newly synthesized peptide may be substantially purified by preparative high performance liquid chromatography (*e.g.*, Creighton, T. (1983) *Proteins, Structures and Molecular Principles*, WH Freeman and Co., New York, N.Y.) or other comparable techniques available in the art. The composition of the synthetic peptides may be confirmed by amino acid analysis or sequencing (*e.g.*, the Edman degradation procedure). Additionally, the amino acid sequence of a polypeptide, or any part thereof, may be altered during direct synthesis and/or combined using chemical methods with sequences from other proteins, or any part thereof, to produce a variant polypeptide.

In order to express a desired polypeptide, the nucleotide sequences encoding the polypeptide, or functional equivalents, may be inserted into appropriate expression vector, *i.e.*, a vector which contains the necessary elements for the transcription and translation of the inserted coding sequence. Methods which are well known to those skilled in the art may be used to construct expression vectors containing sequences encoding a polypeptide of interest and appropriate transcriptional and translational control elements. These methods include *in vitro* recombinant DNA techniques, synthetic techniques, and *in vivo* genetic recombination. Such techniques are described in Sambrook, J. *et al.* (1989) *Molecular Cloning, A Laboratory Manual*, Cold Spring Harbor Press, Plainview, N.Y., and Ausubel, F. M. *et al.* (1989) *Current Protocols in Molecular Biology*, John Wiley & Sons, New York, N.Y.

A variety of expression vector/host systems may be utilized to contain and express polynucleotide sequences. These include, but are not limited to, microorganisms such as bacteria transformed with recombinant bacteriophage, plasmid, or cosmid DNA expression vectors; yeast transformed with yeast expression vectors; insect cell systems
 5 infected with virus expression vectors (*e.g.*, baculovirus); plant cell systems transformed with virus expression vectors (*e.g.*, cauliflower mosaic virus, CaMV; tobacco mosaic virus, TMV) or with bacterial expression vectors (*e.g.*, Ti or pBR322 plasmids); or animal cell systems.

The "control elements" or "regulatory sequences" present in an expression
 10 vector are those non-translated regions of the vector--enhancers, promoters, 5' and 3' untranslated regions--which interact with host cellular proteins to carry out transcription and translation. Such elements may vary in their strength and specificity. Depending on the vector system and host utilized, any number of suitable transcription and translation elements, including constitutive and inducible promoters, may be used. For example, when
 15 cloning in bacterial systems, inducible promoters such as the hybrid lacZ promoter of the PBLUESCRIPT phagemid (Stratagene, La Jolla, Calif.) or PSPORT1 plasmid (Gibco BRL, Gaithersburg, MD) and the like may be used. In mammalian cell systems, promoters from mammalian genes or from mammalian viruses are generally preferred. If it is necessary to generate a cell line that contains multiple copies of the sequence encoding a polypeptide,
 20 vectors based on SV40 or EBV may be advantageously used with an appropriate selectable marker.

In bacterial systems, a number of expression vectors may be selected depending upon the use intended for the expressed polypeptide. For example, when large quantities are needed, for example for the induction of antibodies, vectors which direct
 25 high level expression of fusion proteins that are readily purified may be used. Such vectors include, but are not limited to, the multifunctional *E. coli* cloning and expression vectors such as BLUESCRIPT (Stratagene), in which the sequence encoding the polypeptide of interest may be ligated into the vector in frame with sequences for the amino-terminal Met and the subsequent 7 residues of .beta.-galactosidase so that a hybrid protein is produced;

pIN vectors (Van Heeke, G. and S. M. Schuster (1989) *J. Biol. Chem.* 264:5503-5509); and the like. pGEX Vectors (Promega, Madison, Wis.) may also be used to express foreign polypeptides as fusion proteins with glutathione S-transferase (GST). In general, such fusion proteins are soluble and can easily be purified from lysed cells by adsorption to glutathione-agarose beads followed by elution in the presence of free glutathione. Proteins made in such systems may be designed to include heparin, thrombin, or factor XA protease cleavage sites so that the cloned polypeptide of interest can be released from the GST moiety at will.

In the yeast, *Saccharomyces cerevisiae*, a number of vectors containing constitutive or inducible promoters such as alpha factor, alcohol oxidase, and PGH may be used. For reviews, see Ausubel *et al.* (supra) and Grant *et al.* (1987) *Methods Enzymol.* 153:516-544.

In cases where plant expression vectors are used, the expression of sequences encoding polypeptides may be driven by any of a number of promoters. For example, viral promoters such as the 35S and 19S promoters of CaMV may be used alone or in combination with the omega leader sequence from TMV (Takamatsu, N. (1987) *EMBO J.* 6:307-311. Alternatively, plant promoters such as the small subunit of RUBISCO or heat shock promoters may be used (Coruzzi, G. *et al.* (1984) *EMBO J.* 3:1671-1680; Broglie, R. *et al.* (1984) *Science* 224:838-843; and Winter, J. *et al.* (1991) *Results Probl. Cell Differ.* 17:85-105). These constructs can be introduced into plant cells by direct DNA transformation or pathogen-mediated transfection. Such techniques are described in a number of generally available reviews (see, for example, Hobbs, S. or Murry, L. E. in McGraw Hill Yearbook of Science and Technology (1992) McGraw Hill, New York, N.Y.; pp. 191-196).

An insect system may also be used to express a polypeptide of interest. For example, in one such system, *Autographa californica* nuclear polyhedrosis virus (AcNPV) is used as a vector to express foreign genes in *Spodoptera frugiperda* cells or in *Trichoplusia* larvae. The sequences encoding the polypeptide may be cloned into a non-essential region of the virus, such as the polyhedrin gene, and placed under control of the

polyhedrin promoter. Successful insertion of the polypeptide-encoding sequence will render the polyhedrin gene inactive and produce recombinant virus lacking coat protein. The recombinant viruses may then be used to infect, for example, *S. frugiperda* cells or *Trichoplusia* larvae in which the polypeptide of interest may be expressed (Engelhard, E. K. *et al.* (1994) *Proc. Natl. Acad. Sci.* 91 :3224-3227).

In mammalian host cells, a number of viral-based expression systems are generally available. For example, in cases where an adenovirus is used as an expression vector, sequences encoding a polypeptide of interest may be ligated into an adenovirus transcription/translation complex consisting of the late promoter and tripartite leader sequence. Insertion in a non-essential E1 or E3 region of the viral genome may be used to obtain a viable virus which is capable of expressing the polypeptide in infected host cells (Logan, J. and Shenk, T. (1984) *Proc. Natl. Acad. Sci.* 81:3655-3659). In addition, transcription enhancers, such as the Rous sarcoma virus (RSV) enhancer, may be used to increase expression in mammalian host cells.

Specific initiation signals may also be used to achieve more efficient translation of sequences encoding a polypeptide of interest. Such signals include the ATG initiation codon and adjacent sequences. In cases where sequences encoding the polypeptide, its initiation codon, and upstream sequences are inserted into the appropriate expression vector, no additional transcriptional or translational control signals may be needed. However, in cases where only coding sequence, or a portion thereof, is inserted, exogenous translational control signals including the ATG initiation codon should be provided. Furthermore, the initiation codon should be in the correct reading frame to ensure translation of the entire insert. Exogenous translational elements and initiation codons may be of various origins, both natural and synthetic. The efficiency of expression may be enhanced by the inclusion of enhancers which are appropriate for the particular cell system which is used, such as those described in the literature (Scharf, D. *et al.* (1994) *Results Probl. Cell Differ.* 20:125-162).

In addition, a host cell strain may be chosen for its ability to modulate the expression of the inserted sequences or to process the expressed protein in the desired

fashion. Such modifications of the polypeptide include, but are not limited to, acetylation, carboxylation, glycosylation, phosphorylation, lipidation, and acylation. Post-translational processing which cleaves a "prepro" form of the protein may also be used to facilitate correct insertion, folding and/or function. Different host cells such as CHO, HeLa, MDCK, 5 HEK293, and WI38, which have specific cellular machinery and characteristic mechanisms for such post-translational activities, may be chosen to ensure the correct modification and processing of the foreign protein.

For long-term, high-yield production of recombinant proteins, stable expression is generally preferred. For example, cell lines which stably express a 10 polynucleotide of interest may be transformed using expression vectors which may contain viral origins of replication and/or endogenous expression elements and a selectable marker gene on the same or on a separate vector. Following the introduction of the vector, cells may be allowed to grow for 1-2 days in an enriched media before they are switched to selective media. The purpose of the selectable marker is to confer resistance to selection, 15 and its presence allows growth and recovery of cells which successfully express the introduced sequences. Resistant clones of stably transformed cells may be proliferated using tissue culture techniques appropriate to the cell type.

Any number of selection systems may be used to recover transformed cell lines. These include, but are not limited to, the herpes simplex virus thymidine kinase 20 (Wigler, M. *et al.* (1977) *Cell* 11:223-32) and adenine phosphoribosyltransferase (Lowy, I. *et al.* (1990) *Cell* 22:817-23) genes which can be employed in tk.sup.- or aprt.sup.- cells, respectively. Also, antimetabolite, antibiotic or herbicide resistance can be used as the basis for selection; for example, dhfr which confers resistance to methotrexate (Wigler, M. *et al.* (1980) *Proc. Natl. Acad. Sci.* 77:3567-70); npt, which confers resistance to the 25 aminoglycosides, neomycin and G-418 (Colbere-Garapin, F. *et al.* (1981) *J. Mol. Biol.* 150:1-14); and als or pat, which confer resistance to chlorsulfuron and phosphinotricin acetyltransferase, respectively (Murry, *supra*). Additional selectable genes have been described, for example, trpB, which allows cells to utilize indole in place of tryptophan, or hisD, which allows cells to utilize histinol in place of histidine (Hartman, S. C. and R. C.

Mulligan (1988) *Proc. Natl. Acad. Sci.* 85:8047-51). Recently, the use of visible markers has gained popularity with such markers as anthocyanins, beta-glucuronidase and its substrate GUS, and luciferase and its substrate luciferin, being widely used not only to identify transformants, but also to quantify the amount of transient or stable protein expression attributable to a specific vector system (Rhodes, C. A. *et al.* (1995) *Methods Mol. Biol.* 55:121-131).

Although the presence/absence of marker gene expression suggests that the gene of interest is also present, its presence and expression may need to be confirmed. For example, if the sequence encoding a polypeptide is inserted within a marker gene sequence, recombinant cells containing sequences can be identified by the absence of marker gene function. Alternatively, a marker gene can be placed in tandem with a polypeptide-encoding sequence under the control of a single promoter. Expression of the marker gene in response to induction or selection usually indicates expression of the tandem gene as well.

Alternatively, host cells which contain and express a desired polynucleotide sequence may be identified by a variety of procedures known to those of skill in the art. These procedures include, but are not limited to, DNA-DNA or DNA-RNA hybridizations and protein bioassay or immunoassay techniques which include membrane, solution, or chip based technologies for the detection and/or quantification of nucleic acid or protein.

A variety of protocols for detecting and measuring the expression of polynucleotide-encoded products, using either polyclonal or monoclonal antibodies specific for the product are known in the art. Examples include enzyme-linked immunosorbent assay (ELISA), radioimmunoassay (RIA), and fluorescence activated cell sorting (FACS). A two-site, monoclonal-based immunoassay utilizing monoclonal antibodies reactive to two non-interfering epitopes on a given polypeptide may be preferred for some applications, but a competitive binding assay may also be employed. These and other assays are described, among other places, in Hampton, R. *et al.* (1990; *Serological Methods, a Laboratory Manual*, APS Press, St Paul, Minn.) and Maddox, D. E. *et al.* (1983; *J. Exp. Med.* 158:1211-1216).

A wide variety of labels and conjugation techniques are known by those skilled in the art and may be used in various nucleic acid and amino acid assays. Means for producing labeled hybridization or PCR probes for detecting sequences related to polynucleotides include oligolabeling, nick translation, end-labeling or PCR amplification using a labeled nucleotide. Alternatively, the sequences, or any portions thereof may be cloned into a vector for the production of an mRNA probe. Such vectors are known in the art, are commercially available, and may be used to synthesize RNA probes in vitro by addition of an appropriate RNA polymerase such as T7, T3, or SP6 and labeled nucleotides. These procedures may be conducted using a variety of commercially available kits. Suitable reporter molecules or labels, which may be used include radionuclides, enzymes, fluorescent, chemiluminescent, or chromogenic agents as well as substrates, cofactors, inhibitors, magnetic particles, and the like.

Host cells transformed with a polynucleotide sequence of interest may be cultured under conditions suitable for the expression and recovery of the protein from cell culture. The protein produced by a recombinant cell may be secreted or contained intracellularly depending on the sequence and/or the vector used. As will be understood by those of skill in the art, expression vectors containing polynucleotides of the invention may be designed to contain signal sequences which direct secretion of the encoded polypeptide through a prokaryotic or eukaryotic cell membrane. Other recombinant constructions may be used to join sequences encoding a polypeptide of interest to nucleotide sequence encoding a polypeptide domain which will facilitate purification of soluble proteins. Such purification facilitating domains include, but are not limited to, metal chelating peptides such as histidine-tryptophan modules that allow purification on immobilized metals, protein A domains that allow purification on immobilized immunoglobulin, and the domain utilized in the FLAGS extension/affinity purification system (Immunex Corp., Seattle, Wash.). The inclusion of cleavable linker sequences such as those specific for Factor XA or enterokinase (Invitrogen. San Diego, Calif.) between the purification domain and the encoded polypeptide may be used to facilitate purification. One such expression vector provides for expression of a fusion protein containing a polypeptide of interest and a

nucleic acid encoding 6 histidine residues preceding a thioredoxin or an enterokinase cleavage site. The histidine residues facilitate purification on IMIAC (immobilized metal ion affinity chromatography) as described in Porath, J. *et al.* (1992, *Prot. Exp. Purif.* 3:263-281) while the enterokinase cleavage site provides a means for purifying the desired polypeptide from the fusion protein. A discussion of vectors which contain fusion proteins is provided in Kroll, D. J. *et al.* (1993; *DNA Cell Biol.* 12:441-453).

In addition to recombinant production methods, polypeptides of the invention, and fragments thereof, may be produced by direct peptide synthesis using solid-phase techniques (Merrifield J. (1963) *J. Am. Chem. Soc.* 85:2149-2154). Protein synthesis may be performed using manual techniques or by automation. Automated synthesis may be achieved, for example, using Applied Biosystems 431A Peptide Synthesizer (Perkin Elmer). Alternatively, various fragments may be chemically synthesized separately and combined using chemical methods to produce the full length molecule.

SITE-SPECIFIC MUTAGENESIS

Site-specific mutagenesis is a technique useful in the preparation of individual peptides, or biologically functional equivalent polypeptides, through specific mutagenesis of the underlying polynucleotides that encode them. The technique, well-known to those of skill in the art, further provides a ready ability to prepare and test sequence variants, for example, incorporating one or more of the foregoing considerations, by introducing one or more nucleotide sequence changes into the DNA. Site-specific mutagenesis allows the production of mutants through the use of specific oligonucleotide sequences which encode the DNA sequence of the desired mutation, as well as a sufficient number of adjacent nucleotides, to provide a primer sequence of sufficient size and sequence complexity to form a stable duplex on both sides of the deletion junction being traversed. Mutations may be employed in a selected polynucleotide sequence to improve, alter, decrease, modify, or otherwise change the properties of the polynucleotide itself, and/or alter the properties, activity, composition, stability, or primary sequence of the encoded polypeptide.

In certain embodiments of the present invention, the inventors contemplate the mutagenesis of the disclosed polynucleotide sequences to alter one or more properties of the encoded polypeptide, such as the antigenicity of a polypeptide vaccine. The techniques of site-specific mutagenesis are well-known in the art, and are widely used to
 5 create variants of both polypeptides and polynucleotides. For example, site-specific mutagenesis is often used to alter a specific portion of a DNA molecule. In such embodiments, a primer comprising typically about 14 to about 25 nucleotides or so in length is employed, with about 5 to about 10 residues on both sides of the junction of the sequence being altered.

10 As will be appreciated by those of skill in the art, site-specific mutagenesis techniques have often employed a phage vector that exists in both a single stranded and double stranded form. Typical vectors useful in site-directed mutagenesis include vectors such as the M13 phage. These phage are readily commercially-available and their use is generally well-known to those skilled in the art. Double-stranded plasmids are also
 15 routinely employed in site directed mutagenesis that eliminates the step of transferring the gene of interest from a plasmid to a phage.

In general, site-directed mutagenesis in accordance herewith is performed by first obtaining a single-stranded vector or melting apart of two strands of a double-stranded vector that includes within its sequence a DNA sequence that encodes the
 20 desired peptide. An oligonucleotide primer bearing the desired mutated sequence is prepared, generally synthetically. This primer is then annealed with the single-stranded vector, and subjected to DNA polymerizing enzymes such as *E. coli* polymerase I Klenow fragment, in order to complete the synthesis of the mutation-bearing strand. Thus, a heteroduplex is formed wherein one strand encodes the original non-mutated sequence and
 25 the second strand bears the desired mutation. This heteroduplex vector is then used to transform appropriate cells, such as *E. coli* cells, and clones are selected which include recombinant vectors bearing the mutated sequence arrangement.

The preparation of sequence variants of the selected peptide-encoding DNA segments using site-directed mutagenesis provides a means of producing potentially useful

species and is not meant to be limiting as there are other ways in which sequence variants of peptides and the DNA sequences encoding them may be obtained. For example, recombinant vectors encoding the desired peptide sequence may be treated with mutagenic agents, such as hydroxylamine, to obtain sequence variants. Specific details regarding these methods and protocols are found in the teachings of Maloy *et al.*, 1994; Segal, 1976; Prokop and Bajpai, 1991; Kuby, 1994; and Maniatis *et al.*, 1982, each incorporated herein by reference, for that purpose.

As used herein, the term “oligonucleotide directed mutagenesis procedure” refers to template-dependent processes and vector-mediated propagation which result in an increase in the concentration of a specific nucleic acid molecule relative to its initial concentration, or in an increase in the concentration of a detectable signal, such as amplification. As used herein, the term “oligonucleotide directed mutagenesis procedure” is intended to refer to a process that involves the template-dependent extension of a primer molecule. The term template dependent process refers to nucleic acid synthesis of an RNA or a DNA molecule wherein the sequence of the newly synthesized strand of nucleic acid is dictated by the well-known rules of complementary base pairing (see, for example, Watson, 1987). Typically, vector mediated methodologies involve the introduction of the nucleic acid fragment into a DNA or RNA vector, the clonal amplification of the vector, and the recovery of the amplified nucleic acid fragment. Examples of such methodologies are provided by U. S. Patent No. 4,237,224, specifically incorporated herein by reference in its entirety.

POLYNUCLEOTIDE AMPLIFICATION TECHNIQUES

A number of template dependent processes are available to amplify the target sequences of interest present in a sample. One of the best known amplification methods is the polymerase chain reaction (PCR™) which is described in detail in U.S. Patent Nos. 4,683,195, 4,683,202 and 4,800,159, each of which is incorporated herein by reference in its entirety. Briefly, in PCR™, two primer sequences are prepared which are complementary to regions on opposite complementary strands of the target sequence. An

excess of deoxynucleoside triphosphates is added to a reaction mixture along with a DNA polymerase (*e.g.*, *Taq* polymerase). If the target sequence is present in a sample, the primers will bind to the target and the polymerase will cause the primers to be extended along the target sequence by adding on nucleotides. By raising and lowering the temperature of the reaction mixture, the extended primers will dissociate from the target to form reaction products, excess primers will bind to the target and to the reaction product and the process is repeated. Preferably reverse transcription and PCRTM amplification procedure may be performed in order to quantify the amount of mRNA amplified. Polymerase chain reaction methodologies are well known in the art.

Another method for amplification is the ligase chain reaction (referred to as LCR), disclosed in Eur. Pat. Appl. Publ. No. 320,308 (specifically incorporated herein by reference in its entirety). In LCR, two complementary probe pairs are prepared, and in the presence of the target sequence, each pair will bind to opposite complementary strands of the target such that they abut. In the presence of a ligase, the two probe pairs will link to form a single unit. By temperature cycling, as in PCRTM, bound ligated units dissociate from the target and then serve as "target sequences" for ligation of excess probe pairs. U.S. Patent No. 4,883,750, incorporated herein by reference in its entirety, describes an alternative method of amplification similar to LCR for binding probe pairs to a target sequence.

Qbeta Replicase, described in PCT Intl. Pat. Appl. Publ. No. PCT/US87/00880, incorporated herein by reference in its entirety, may also be used as still another amplification method in the present invention. In this method, a replicative sequence of RNA that has a region complementary to that of a target is added to a sample in the presence of an RNA polymerase. The polymerase will copy the replicative sequence that can then be detected.

An isothermal amplification method, in which restriction endonucleases and ligases are used to achieve the amplification of target molecules that contain nucleotide 5'-[α -thio]triphosphates in one strand of a restriction site (Walker *et al.*, 1992, incorporated

herein by reference in its entirety), may also be useful in the amplification of nucleic acids in the present invention.

Strand Displacement Amplification (SDA) is another method of carrying out isothermal amplification of nucleic acids which involves multiple rounds of strand displacement and synthesis, *i.e.* nick translation. A similar method, called Repair Chain Reaction (RCR) is another method of amplification which may be useful in the present invention and is involves annealing several probes throughout a region targeted for amplification, followed by a repair reaction in which only two of the four bases are present. The other two bases can be added as biotinylated derivatives for easy detection. A similar approach is used in SDA.

Sequences can also be detected using a cyclic probe reaction (CPR). In CPR, a probe having a 3' and 5' sequences of non-target DNA and an internal or "middle" sequence of the target protein specific RNA is hybridized to DNA which is present in a sample. Upon hybridization, the reaction is treated with RNaseH, and the products of the probe are identified as distinctive products by generating a signal that is released after digestion. The original template is annealed to another cycling probe and the reaction is repeated. Thus, CPR involves amplifying a signal generated by hybridization of a probe to a target gene specific expressed nucleic acid.

Still other amplification methods described in Great Britain Pat. Appl. No. 2 202 328, and in PCT Intl. Pat. Appl. Publ. No. PCT/US89/01025, each of which is incorporated herein by reference in its entirety, may be used in accordance with the present invention. In the former application, "modified" primers are used in a PCR-like, template and enzyme dependent synthesis. The primers may be modified by labeling with a capture moiety (*e.g.*, biotin) and/or a detector moiety (*e.g.*, enzyme). In the latter application, an excess of labeled probes is added to a sample. In the presence of the target sequence, the probe binds and is cleaved catalytically. After cleavage, the target sequence is released intact to be bound by excess probe. Cleavage of the labeled probe signals the presence of the target sequence.

Other nucleic acid amplification procedures include transcription-based amplification systems (TAS) (Kwoh *et al.*, 1989; PCT Intl. Pat. Appl. Publ. No. WO 88/10315, incorporated herein by reference in its entirety), including nucleic acid sequence based amplification (NASBA) and 3SR. In NASBA, the nucleic acids can be prepared for

5 amplification by standard phenol/chloroform extraction, heat denaturation of a sample, treatment with lysis buffer and minispin columns for isolation of DNA and RNA or guanidinium chloride extraction of RNA. These amplification techniques involve annealing a primer that has sequences specific to the target sequence. Following polymerization, DNA/RNA hybrids are digested with RNase H while double stranded

10 DNA molecules are heat-denatured again. In either case the single stranded DNA is made fully double stranded by addition of second target-specific primer, followed by polymerization. The double stranded DNA molecules are then multiply transcribed by a polymerase such as T7 or SP6. In an isothermal cyclic reaction, the RNAs are reverse transcribed into DNA, and transcribed once again with a polymerase such as T7 or SP6.

15 The resulting products, whether truncated or complete, indicate target-specific sequences.

Eur. Pat. Appl. Publ. No. 329,822, incorporated herein by reference in its entirety, disclose a nucleic acid amplification process involving cyclically synthesizing single-stranded RNA ("ssRNA"), ssDNA, and double-stranded DNA (dsDNA), which may be used in accordance with the present invention. The ssRNA is a first template for a first

20 primer oligonucleotide, which is elongated by reverse transcriptase (RNA-dependent DNA polymerase). The RNA is then removed from resulting DNA:RNA duplex by the action of ribonuclease H (RNase H, an RNase specific for RNA in a duplex with either DNA or RNA). The resultant ssDNA is a second template for a second primer, which also includes the sequences of an RNA polymerase promoter (exemplified by T7 RNA polymerase) 5' to

25 its homology to its template. This primer is then extended by DNA polymerase (exemplified by the large "Klenow" fragment of *E. coli* DNA polymerase I), resulting as a double-stranded DNA ("dsDNA") molecule, having a sequence identical to that of the original RNA between the primers and having additionally, at one end, a promoter sequence. This promoter sequence can be used by the appropriate RNA polymerase to

make many RNA copies of the DNA. These copies can then re-enter the cycle leading to very swift amplification. With proper choice of enzymes, this amplification can be done isothermally without addition of enzymes at each cycle. Because of the cyclical nature of this process, the starting sequence can be chosen to be in the form of either DNA or RNA.

5 PCT Intl. Pat. Appl. Publ. No. WO 89/06700, incorporated herein by reference in its entirety, disclose a nucleic acid sequence amplification scheme based on the hybridization of a promoter/primer sequence to a target single-stranded DNA ("ssDNA") followed by transcription of many RNA copies of the sequence. This scheme is not cyclic; *i.e.* new templates are not produced from the resultant RNA transcripts. Other
10 amplification methods include "RACE" (Frohman, 1990), and "one-sided PCR" (Ohara, 1989) which are well-known to those of skill in the art.

Methods based on ligation of two (or more) oligonucleotides in the presence of nucleic acid having the sequence of the resulting "di-oligonucleotide", thereby amplifying the di-oligonucleotide (Wu and Dean, 1996, incorporated herein by reference in
15 its entirety), may also be used in the amplification of DNA sequences of the present invention.

BIOLOGICAL FUNCTIONAL EQUIVALENTS

Modification and changes may be made in the structure of the polynucleotides and polypeptides of the present invention and still obtain a functional
20 molecule that encodes a polypeptide with desirable characteristics. As mentioned above, it is often desirable to introduce one or more mutations into a specific polynucleotide sequence. In certain circumstances, the resulting encoded polypeptide sequence is altered by this mutation, or in other cases, the sequence of the polypeptide is unchanged by one or more mutations in the encoding polynucleotide.

25 When it is desirable to alter the amino acid sequence of a polypeptide to create an equivalent, or even an improved, second-generation molecule, the amino acid changes may be achieved by changing one or more of the codons of the encoding DNA sequence, according to Table 1.

For example, certain amino acids may be substituted for other amino acids in a protein structure without appreciable loss of interactive binding capacity with structures such as, for example, antigen-binding regions of antibodies or binding sites on substrate molecules. Since it is the interactive capacity and nature of a protein that defines that protein's biological functional activity, certain amino acid sequence substitutions can be made in a protein sequence, and, of course, its underlying DNA coding sequence, and nevertheless obtain a protein with like properties. It is thus contemplated by the inventors that various changes may be made in the peptide sequences of the disclosed compositions, or corresponding DNA sequences which encode said peptides without appreciable loss of their biological utility or activity.

TABLE 1

Amino Acids			Codons					
Alanine	Ala	A	GCA	GCC	GCG	GCU		
Cysteine	Cys	C	UGC	UGU				
Aspartic acid	Asp	D	GAC	GAU				
Glutamic acid	Glu	E	GAA	GAG				
Phenylalanine	Phe	F	UUC	UUU				
Glycine	Gly	G	GGA	GGC	GGG	GGU		
Histidine	His	H	CAC	CAU				
Isoleucine	Ile	I	AUA	AUC	AUU			
Lysine	Lys	K	AAA	AAG				
Leucine	Leu	L	UUA	UUG	CUA	CUC	CUG	CUU
Methionine	Met	M	AUG					
Asparagine	Asn	N	AAC	AAU				
Proline	Pro	P	CCA	CCC	CCG	CCU		
Glutamine	Gln	Q	CAA	CAG				
Arginine	Arg	R	AGA	AGG	CGA	CGC	CGG	CGU
Serine	Ser	S	AGC	AGU	UCA	UCC	UCG	UCU
Threonine	Thr	T	ACA	ACC	ACG	ACU		
Valine	Val	V	GUA	GUC	GUG	GUU		
Tryptophan	Trp	W	UGG					
Tyrosine	Tyr	Y	UAC	UAU				

In making such changes, the hydropathic index of amino acids may be considered. The importance of the hydropathic amino acid index in conferring interactive biologic function on a protein is generally understood in the art (Kyte and Doolittle, 1982, incorporated herein by reference). It is accepted that the relative hydropathic character of the amino acid contributes to the secondary structure of the resultant protein, which in turn defines the interaction of the protein with other molecules, for example, enzymes, substrates, receptors, DNA, antibodies, antigens, and the like. Each amino acid has been

assigned a hydropathic index on the basis of its hydrophobicity and charge characteristics (Kyte and Doolittle, 1982). These values are: isoleucine (+4.5); valine (+4.2); leucine (+3.8); phenylalanine (+2.8); cysteine/cystine (+2.5); methionine (+1.9); alanine (+1.8); glycine (−0.4); threonine (−0.7); serine (−0.8); tryptophan (−0.9); tyrosine (−1.3); proline (−1.6); histidine (−3.2); glutamate (−3.5); glutamine (−3.5); aspartate (−3.5); asparagine (−3.5); lysine (−3.9); and arginine (−4.5).

It is known in the art that certain amino acids may be substituted by other amino acids having a similar hydropathic index or score and still result in a protein with similar biological activity, *i.e.* still obtain a biological functionally equivalent protein. In making such changes, the substitution of amino acids whose hydropathic indices are within ± 2 is preferred, those within ± 1 are particularly preferred, and those within ± 0.5 are even more particularly preferred. It is also understood in the art that the substitution of like amino acids can be made effectively on the basis of hydrophilicity. U. S. Patent 4,554,101 (specifically incorporated herein by reference in its entirety), states that the greatest local average hydrophilicity of a protein, as governed by the hydrophilicity of its adjacent amino acids, correlates with a biological property of the protein.

As detailed in U. S. Patent 4,554,101, the following hydrophilicity values have been assigned to amino acid residues: arginine (+3.0); lysine (+3.0); aspartate (+3.0 \pm 1); glutamate (+3.0 \pm 1); serine (+0.3); asparagine (+0.2); glutamine (+0.2); glycine (0); threonine (−0.4); proline (−0.5 \pm 1); alanine (−0.5); histidine (−0.5); cysteine (−1.0); methionine (−1.3); valine (−1.5); leucine (−1.8); isoleucine (−1.8); tyrosine (−2.3); phenylalanine (−2.5); tryptophan (−3.4). It is understood that an amino acid can be substituted for another having a similar hydrophilicity value and still obtain a biologically equivalent, and in particular, an immunologically equivalent protein. In such changes, the substitution of amino acids whose hydrophilicity values are within ± 2 is preferred, those within ± 1 are particularly preferred, and those within ± 0.5 are even more particularly preferred.

As outlined above, amino acid substitutions are generally therefore based on the relative similarity of the amino acid side-chain substituents, for example, their

5 In addition, any polynucleotide may be further modified to increase stability
in vivo. Possible modifications include, but are not limited to, the addition of flanking
sequences at the 5' and/or 3' ends; the use of phosphorothioate or 2' O-methyl rather than
phosphodiesterase linkages in the backbone; and/or the inclusion of nontraditional bases
such as inosine, queosine and wybutosine, as well as acetyl- methyl-, thio- and other
10 modified forms of adenine, cytidine, guanine, thymine and uridine.

In additional embodiments, genetic constructs comprising one or more of the polynucleotides of the invention are introduced into cells *in vivo*. This may be achieved using any of a variety of well known approaches, several of which are outlined below for the purpose of illustration.

One of the preferred methods for *in vivo* delivery of one or more nucleic acid sequences involves the use of an adenovirus expression vector. "Adenovirus expression vector" is meant to include those constructs containing adenovirus sequences sufficient to (a) support packaging of the construct and (b) to express a polynucleotide that has been cloned therein in a sense or antisense orientation. Of course, in the context of an antisense construct, expression does not require that the gene product be synthesized.

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adenoviral DNA can replicate in an episomal manner without potential genotoxicity. Also, adenoviruses are structurally stable, and no genome rearrangement has been detected after extensive amplification. Adenovirus can infect virtually all epithelial cells regardless of their cell cycle stage. So far, adenoviral infection appears to be linked only to mild disease
 5 such as acute respiratory disease in humans.

Adenovirus is particularly suitable for use as a gene transfer vector because of its mid-sized genome, ease of manipulation, high titer, wide target-cell range and high infectivity. Both ends of the viral genome contain 100-200 base pair inverted repeats (ITRs), which are *cis* elements necessary for viral DNA replication and packaging. The
 10 early (E) and late (L) regions of the genome contain different transcription units that are divided by the onset of viral DNA replication. The E1 region (E1A and E1B) encodes proteins responsible for the regulation of transcription of the viral genome and a few cellular genes. The expression of the E2 region (E2A and E2B) results in the synthesis of the proteins for viral DNA replication. These proteins are involved in DNA replication,
 15 late gene expression and host cell shut-off (Renan, 1990). The products of the late genes, including the majority of the viral capsid proteins, are expressed only after significant processing of a single primary transcript issued by the major late promoter (MLP). The MLP, (located at 16.8 m.u.) is particularly efficient during the late phase of infection, and all the mRNA's issued from this promoter possess a 5'-tripartite leader (TPL) sequence
 20 which makes them preferred mRNA's for translation.

In a current system, recombinant adenovirus is generated from homologous recombination between shuttle vector and provirus vector. Due to the possible recombination between two proviral vectors, wild-type adenovirus may be generated from this process. Therefore, it is critical to isolate a single clone of virus from an individual
 25 plaque and examine its genomic structure.

Generation and propagation of the current adenovirus vectors, which are replication deficient, depend on a unique helper cell line, designated 293, which was transformed from human embryonic kidney cells by Ad5 DNA fragments and constitutively expresses E1 proteins (Graham *et al.*, 1977). Since the E3 region is

dispensable from the adenovirus genome (Jones and Shenk, 1978), the current adenovirus vectors, with the help of 293 cells, carry foreign DNA in either the E1, the D3 or both regions (Graham and Prevec, 1991). In nature, adenovirus can package approximately 105% of the wild-type genome (Ghosh-Choudhury *et al.*, 1987), providing capacity for about 2 extra kB of DNA. Combined with the approximately 5.5 kB of DNA that is replaceable in the E1 and E3 regions, the maximum capacity of the current adenovirus vector is under 7.5 kB, or about 15% of the total length of the vector. More than 80% of the adenovirus viral genome remains in the vector backbone and is the source of vector-borne cytotoxicity. Also, the replication deficiency of the E1-deleted virus is incomplete.

For example, leakage of viral gene expression has been observed with the currently available vectors at high multiplicities of infection (MOI) (Mulligan, 1993).

Helper cell lines may be derived from human cells such as human embryonic kidney cells, muscle cells, hematopoietic cells or other human embryonic mesenchymal or epithelial cells. Alternatively, the helper cells may be derived from the cells of other mammalian species that are permissive for human adenovirus. Such cells include, *e.g.*, Vero cells or other monkey embryonic mesenchymal or epithelial cells. As stated above, the currently preferred helper cell line is 293.

Recently, Racher *et al.* (1995) disclosed improved methods for culturing 293 cells and propagating adenovirus. In one format, natural cell aggregates are grown by inoculating individual cells into 1 liter siliconized spinner flasks (Techne, Cambridge, UK) containing 100-200 ml of medium. Following stirring at 40 rpm, the cell viability is estimated with trypan blue. In another format, Fibra-Cel microcarriers (Bibby Sterlin, Stone, UK) (5 g/l) is employed as follows. A cell inoculum, resuspended in 5 ml of medium, is added to the carrier (50 ml) in a 250 ml Erlenmeyer flask and left stationary, with occasional agitation, for 1 to 4 h. The medium is then replaced with 50 ml of fresh medium and shaking initiated. For virus production, cells are allowed to grow to about 80% confluence, after which time the medium is replaced (to 25% of the final volume) and adenovirus added at an MOI of 0.05. Cultures are left stationary overnight, following which the volume is increased to 100% and shaking commenced for another 72 h.

Other than the requirement that the adenovirus vector be replication defective, or at least conditionally defective, the nature of the adenovirus vector is not believed to be crucial to the successful practice of the invention. The adenovirus may be of any of the 42 different known serotypes or subgroups A-F. Adenovirus type 5 of subgroup
 5 C is the preferred starting material in order to obtain a conditional replication-defective adenovirus vector for use in the present invention, since Adenovirus type 5 is a human adenovirus about which a great deal of biochemical and genetic information is known, and it has historically been used for most constructions employing adenovirus as a vector.

As stated above, the typical vector according to the present invention is
 10 replication defective and will not have an adenovirus E1 region. Thus, it will be most convenient to introduce the polynucleotide encoding the gene of interest at the position from which the E1-coding sequences have been removed. However, the position of insertion of the construct within the adenovirus sequences is not critical to the invention. The polynucleotide encoding the gene of interest may also be inserted in lieu of the deleted
 15 E3 region in E3 replacement vectors as described by Karlsson *et al.* (1986) or in the E4 region where a helper cell line or helper virus complements the E4 defect.

Adenovirus is easy to grow and manipulate and exhibits broad host range *in vitro* and *in vivo*. This group of viruses can be obtained in high titers, *e.g.*, 10^9 - 10^{11} plaque-forming units per ml, and they are highly infective. The life cycle of adenovirus does not
 20 require integration into the host cell genome. The foreign genes delivered by adenovirus vectors are episomal and, therefore, have low genotoxicity to host cells. No side effects have been reported in studies of vaccination with wild-type adenovirus (Couch *et al.*, 1963; Top *et al.*, 1971), demonstrating their safety and therapeutic potential as *in vivo* gene transfer vectors.

25 Adenovirus vectors have been used in eukaryotic gene expression (Levrero *et al.*, 1991; Gomez-Foix *et al.*, 1992) and vaccine development (Grunhaus and Horwitz, 1992; Graham and Prevec, 1992). Recently, animal studies suggested that recombinant adenovirus could be used for gene therapy (Stratford-Perricaudet and Perricaudet, 1991; Stratford-Perricaudet *et al.*, 1990; Rich *et al.*, 1993). Studies in administering recombinant

adenovirus to different tissues include trachea instillation (Rosenfeld *et al.*, 1991; Rosenfeld *et al.*, 1992), muscle injection (Ragot *et al.*, 1993), peripheral intravenous injections (Herz and Gerard, 1993) and stereotactic inoculation into the brain (Le Gal La Salle *et al.*, 1993).

5 2. RETROVIRUSES

The retroviruses are a group of single-stranded RNA viruses characterized by an ability to convert their RNA to double-stranded DNA in infected cells by a process of reverse-transcription (Coffin, 1990). The resulting DNA then stably integrates into cellular chromosomes as a provirus and directs synthesis of viral proteins. The integration results
10 in the retention of the viral gene sequences in the recipient cell and its descendants. The retroviral genome contains three genes, gag, pol, and env that code for capsid proteins, polymerase enzyme, and envelope components, respectively. A sequence found upstream from the gag gene contains a signal for packaging of the genome into virions. Two long terminal repeat (LTR) sequences are present at the 5' and 3' ends of the viral genome.
15 These contain strong promoter and enhancer sequences and are also required for integration in the host cell genome (Coffin, 1990).

In order to construct a retroviral vector, a nucleic acid encoding one or more oligonucleotide or polynucleotide sequences of interest is inserted into the viral genome in the place of certain viral sequences to produce a virus that is replication-defective. In order
20 to produce virions, a packaging cell line containing the gag, pol, and env genes but without the LTR and packaging components is constructed (Mann *et al.*, 1983). When a recombinant plasmid containing a cDNA, together with the retroviral LTR and packaging sequences is introduced into this cell line (by calcium phosphate precipitation for example), the packaging sequence allows the RNA transcript of the recombinant plasmid to be
25 packaged into viral particles, which are then secreted into the culture media (Nicolas and Rubenstein, 1988; Temin, 1986; Mann *et al.*, 1983). The media containing the recombinant retroviruses is then collected, optionally concentrated, and used for gene

transfer. Retroviral vectors are able to infect a broad variety of cell types. However, integration and stable expression require the division of host cells (Paskind *et al.*, 1975).

A novel approach designed to allow specific targeting of retrovirus vectors was recently developed based on the chemical modification of a retrovirus by the chemical addition of lactose residues to the viral envelope. This modification could permit the specific infection of hepatocytes *via* sialoglycoprotein receptors.

A different approach to targeting of recombinant retroviruses was designed in which biotinylated antibodies against a retroviral envelope protein and against a specific cell receptor were used. The antibodies were coupled *via* the biotin components by using streptavidin (Roux *et al.*, 1989). Using antibodies against major histocompatibility complex class I and class II antigens, they demonstrated the infection of a variety of human cells that bore those surface antigens with an ecotropic virus *in vitro* (Roux *et al.*, 1989).

3. ADENO-ASSOCIATED VIRUSES

AAV (Ridgeway, 1988; Hermonat and Muzyczka, 1984) is a parovirus, discovered as a contamination of adenoviral stocks. It is a ubiquitous virus (antibodies are present in 85% of the US human population) that has not been linked to any disease. It is also classified as a dependovirus, because its replications is dependent on the presence of a helper virus, such as adenovirus. Five serotypes have been isolated, of which AAV-2 is the best characterized. AAV has a single-stranded linear DNA that is encapsidated into capsid proteins VP1, VP2 and VP3 to form an icosahedral virion of 20 to 24 nm in diameter (Muzyczka and McLaughlin, 1988).

The AAV DNA is approximately 4.7 kilobases long. It contains two open reading frames and is flanked by two ITRs. There are two major genes in the AAV genome: *rep* and *cap*. The *rep* gene codes for proteins responsible for viral replications, whereas *cap* codes for capsid protein VP1-3. Each ITR forms a T-shaped hairpin structure. These terminal repeats are the only essential *cis* components of the AAV for chromosomal integration. Therefore, the AAV can be used as a vector with all viral coding sequences removed and replaced by the cassette of genes for delivery. Three viral

promoters have been identified and named p5, p19, and p40, according to their map position. Transcription from p5 and p19 results in production of rep proteins, and transcription from p40 produces the capsid proteins (Hermonat and Muzyczka, 1984).

There are several factors that prompted researchers to study the possibility of using rAAV as an expression vector. One is that the requirements for delivering a gene to integrate into the host chromosome are surprisingly few. It is necessary to have the 145-bp ITRs, which are only 6% of the AAV genome. This leaves room in the vector to assemble a 4.5-kb DNA insertion. While this carrying capacity may prevent the AAV from delivering large genes, it is amply suited for delivering the antisense constructs of the present invention.

AAV is also a good choice of delivery vehicles due to its safety. There is a relatively complicated rescue mechanism: not only wild type adenovirus but also AAV genes are required to mobilize rAAV. Likewise, AAV is not pathogenic and not associated with any disease. The removal of viral coding sequences minimizes immune reactions to viral gene expression, and therefore, rAAV does not evoke an inflammatory response.

4. OTHER VIRAL VECTORS AS EXPRESSION CONSTRUCTS

Other viral vectors may be employed as expression constructs in the present invention for the delivery of oligonucleotide or polynucleotide sequences to a host cell. Vectors derived from viruses such as vaccinia virus (Ridgeway, 1988; Coupar *et al.*, 1988), lentiviruses, polio viruses and herpes viruses may be employed. They offer several attractive features for various mammalian cells (Friedmann, 1989; Ridgeway, 1988; Coupar *et al.*, 1988; Horwich *et al.*, 1990).

With the recent recognition of defective hepatitis B viruses, new insight was gained into the structure-function relationship of different viral sequences. *In vitro* studies showed that the virus could retain the ability for helper-dependent packaging and reverse transcription despite the deletion of up to 80% of its genome (Horwich *et al.*, 1990). This suggested that large portions of the genome could be replaced with foreign genetic material. The hepatotropism and persistence (integration) were particularly attractive

properties for liver-directed gene transfer. Chang *et al.* (1991) introduced the chloramphenicol acetyltransferase (CAT) gene into duck hepatitis B virus genome in the place of the polymerase, surface, and pre-surface coding sequences. It was cotransfected with wild-type virus into an avian hepatoma cell line. Culture media containing high titers of the recombinant virus were used to infect primary duckling hepatocytes. Stable CAT gene expression was detected for at least 24 days after transfection (Chang *et al.*, 1991).

5. NON-VIRAL VECTORS

In order to effect expression of the oligonucleotide or polynucleotide sequences of the present invention, the expression construct must be delivered into a cell. This delivery may be accomplished *in vitro*, as in laboratory procedures for transforming cells lines, or *in vivo* or *ex vivo*, as in the treatment of certain disease states. As described above, one preferred mechanism for delivery is *via* viral infection where the expression construct is encapsulated in an infectious viral particle.

Once the expression construct has been delivered into the cell the nucleic acid encoding the desired oligonucleotide or polynucleotide sequences may be positioned and expressed at different sites. In certain embodiments, the nucleic acid encoding the construct may be stably integrated into the genome of the cell. This integration may be in the specific location and orientation *via* homologous recombination (gene replacement) or it may be integrated in a random, non-specific location (gene augmentation). In yet further embodiments, the nucleic acid may be stably maintained in the cell as a separate, episomal segment of DNA. Such nucleic acid segments or "episomes" encode sequences sufficient to permit maintenance and replication independent of or in synchronization with the host cell cycle. How the expression construct is delivered to a cell and where in the cell the nucleic acid remains is dependent on the type of expression construct employed.

In certain embodiments of the invention, the expression construct comprising one or more oligonucleotide or polynucleotide sequences may simply consist of naked recombinant DNA or plasmids. Transfer of the construct may be performed by any of the methods mentioned above which physically or chemically permeabilize the cell

membrane. This is particularly applicable for transfer *in vitro* but it may be applied to *in vivo* use as well. Dubensky *et al.* (1984) successfully injected polyomavirus DNA in the form of calcium phosphate precipitates into liver and spleen of adult and newborn mice demonstrating active viral replication and acute infection. Benvenisty and Reshef (1986) also demonstrated that direct intraperitoneal injection of calcium phosphate-precipitated plasmids results in expression of the transfected genes. It is envisioned that DNA encoding a gene of interest may also be transferred in a similar manner *in vivo* and express the gene product.

Another embodiment of the invention for transferring a naked DNA expression construct into cells may involve particle bombardment. This method depends on the ability to accelerate DNA-coated microprojectiles to a high velocity allowing them to pierce cell membranes and enter cells without killing them (Klein *et al.*, 1987). Several devices for accelerating small particles have been developed. One such device relies on a high voltage discharge to generate an electrical current, which in turn provides the motive force (Yang *et al.*, 1990). The microprojectiles used have consisted of biologically inert substances such as tungsten or gold beads.

Selected organs including the liver, skin, and muscle tissue of rats and mice have been bombarded *in vivo* (Yang *et al.*, 1990; Zelenin *et al.*, 1991). This may require surgical exposure of the tissue or cells, to eliminate any intervening tissue between the gun and the target organ, *i.e.* *ex vivo* treatment. Again, DNA encoding a particular gene may be delivered *via* this method and still be incorporated by the present invention.

ANTISENSE OLIGONUCLEOTIDES

The end result of the flow of genetic information is the synthesis of protein. DNA is transcribed by polymerases into messenger RNA and translated on the ribosome to yield a folded, functional protein. Thus there are several steps along the route where protein synthesis can be inhibited. The native DNA segment coding for a polypeptide described herein, as all such mammalian DNA strands, has two strands: a sense strand and an antisense strand held together by hydrogen bonding. The messenger RNA coding for

polypeptide has the same nucleotide sequence as the sense DNA strand except that the DNA thymidine is replaced by uridine. Thus, synthetic antisense nucleotide sequences will bind to a mRNA and inhibit expression of the protein encoded by that mRNA.

The targeting of antisense oligonucleotides to mRNA is thus one mechanism
 5 to shut down protein synthesis, and, consequently, represents a powerful and targeted therapeutic approach. For example, the synthesis of polygalacturonase and the muscarine type 2 acetylcholine receptor are inhibited by antisense oligonucleotides directed to their respective mRNA sequences (U. S. Patent 5,739,119 and U. S. Patent 5,759,829, each specifically incorporated herein by reference in its entirety). Further, examples of antisense
 10 inhibition have been demonstrated with the nuclear protein cyclin, the multiple drug resistance gene (MDG1), ICAM-1, E-selectin, STK-1, striatal GABA_A receptor and human EGF (Jaskulski *et al.*, 1988; Vasanthakumar and Ahmed, 1989; Peris *et al.*, 1998; U. S. Patent 5,801,154; U. S. Patent 5,789,573; U. S. Patent 5,718,709 and U. S. Patent 5,610,288, each specifically incorporated herein by reference in its entirety). Antisense
 15 constructs have also been described that inhibit and can be used to treat a variety of abnormal cellular proliferations, *e.g.* cancer (U. S. Patent 5,747,470; U. S. Patent 5,591,317 and U. S. Patent 5,783,683, each specifically incorporated herein by reference in its entirety).

Therefore, in exemplary embodiments, the invention provides
 20 oligonucleotide sequences that comprise all, or a portion of, any sequence that is capable of specifically binding to polynucleotide sequence described herein, or a complement thereof. In one embodiment, the antisense oligonucleotides comprise DNA or derivatives thereof. In another embodiment, the oligonucleotides comprise RNA or derivatives thereof. In a third embodiment, the oligonucleotides are modified DNAs comprising a
 25 phosphorothioated modified backbone. In a fourth embodiment, the oligonucleotide sequences comprise peptide nucleic acids or derivatives thereof. In each case, preferred compositions comprise a sequence region that is complementary, and more preferably substantially-complementary, and even more preferably, completely complementary to one or more portions of polynucleotides disclosed herein.

Selection of antisense compositions specific for a given gene sequence is based upon analysis of the chosen target sequence (*i.e.* in these illustrative examples the rat and human sequences) and determination of secondary structure, T_m , binding energy, relative stability, and antisense compositions were selected based upon their relative
 5 inability to form dimers, hairpins, or other secondary structures that would reduce or prohibit specific binding to the target mRNA in a host cell.

Highly preferred target regions of the mRNA, are those which are at or near the AUG translation initiation codon, and those sequences which were substantially complementary to 5' regions of the mRNA. These secondary structure analyses and target
 10 site selection considerations were performed using v.4 of the OLIGO primer analysis software (Rychlik, 1997) and the BLASTN 2.0.5 algorithm software (Altschul *et al.*, 1997).

The use of an antisense delivery method employing a short peptide vector, termed MPG (27 residues), is also contemplated. The MPG peptide contains a hydrophobic domain derived from the fusion sequence of HIV gp41 and a hydrophilic
 15 domain from the nuclear localization sequence of SV40 T-antigen (Morris *et al.*, 1997). It has been demonstrated that several molecules of the MPG peptide coat the antisense oligonucleotides and can be delivered into cultured mammalian cells in less than 1 hour with relatively high efficiency (90%). Further, the interaction with MPG strongly increases both the stability of the oligonucleotide to nuclease and the ability to cross the plasma
 20 membrane (Morris *et al.*, 1997).

RIBOZYMES

Although proteins traditionally have been used for catalysis of nucleic acids, another class of macromolecules has emerged as useful in this endeavor. Ribozymes are RNA-protein complexes that cleave nucleic acids in a site-specific fashion. Ribozymes
 25 have specific catalytic domains that possess endonuclease activity (Kim and Cech, 1987; Gerlach *et al.*, 1987; Forster and Symons, 1987). For example, a large number of ribozymes accelerate phosphoester transfer reactions with a high degree of specificity, often cleaving only one of several phosphoesters in an oligonucleotide substrate (Cech *et*

al., 1981; Michel and Westhof, 1990; Reinhold-Hurek and Shub, 1992). This specificity has been attributed to the requirement that the substrate bind via specific base-pairing interactions to the internal guide sequence ("IGS") of the ribozyme prior to chemical reaction.

5 Ribozyme catalysis has primarily been observed as part of sequence-specific cleavage/ligation reactions involving nucleic acids (Joyce, 1989; Cech *et al.*, 1981). For example, U. S. Patent No. 5,354,855 (specifically incorporated herein by reference) reports that certain ribozymes can act as endonucleases with a sequence specificity greater than that of known ribonucleases and approaching that of the DNA restriction enzymes. Thus, 10 sequence-specific ribozyme-mediated inhibition of gene expression may be particularly suited to therapeutic applications (Scanlon *et al.*, 1991; Sarver *et al.*, 1990). Recently, it was reported that ribozymes elicited genetic changes in some cells lines to which they were applied; the altered genes included the oncogenes *H-ras*, *c-fos* and genes of HIV. Most of this work involved the modification of a target mRNA, based on a specific mutant codon 15 that is cleaved by a specific ribozyme.

 Six basic varieties of naturally-occurring enzymatic RNAs are known presently. Each can catalyze the hydrolysis of RNA phosphodiester bonds *in trans* (and thus can cleave other RNA molecules) under physiological conditions. In general, enzymatic nucleic acids act by first binding to a target RNA. Such binding occurs through 20 the target binding portion of a enzymatic nucleic acid which is held in close proximity to an enzymatic portion of the molecule that acts to cleave the target RNA. Thus, the enzymatic nucleic acid first recognizes and then binds a target RNA through complementary base-pairing, and once bound to the correct site, acts enzymatically to cut the target RNA. Strategic cleavage of such a target RNA will destroy its ability to direct synthesis of an 25 encoded protein. After an enzymatic nucleic acid has bound and cleaved its RNA target, it is released from that RNA to search for another target and can repeatedly bind and cleave new targets.

 The enzymatic nature of a ribozyme is advantageous over many technologies, such as antisense technology (where a nucleic acid molecule simply binds to

a nucleic acid target to block its translation) since the concentration of ribozyme necessary to affect a therapeutic treatment is lower than that of an antisense oligonucleotide. This advantage reflects the ability of the ribozyme to act enzymatically. Thus, a single ribozyme molecule is able to cleave many molecules of target RNA. In addition, the
 5 ribozyme is a highly specific inhibitor, with the specificity of inhibition depending not only on the base pairing mechanism of binding to the target RNA, but also on the mechanism of target RNA cleavage. Single mismatches, or base-substitutions, near the site of cleavage can completely eliminate catalytic activity of a ribozyme. Similar mismatches in antisense molecules do not prevent their action (Woolf *et al.*, 1992). Thus, the specificity of action
 10 of a ribozyme is greater than that of an antisense oligonucleotide binding the same RNA site.

The enzymatic nucleic acid molecule may be formed in a hammerhead, hairpin, a hepatitis δ virus, group I intron or RNaseP RNA (in association with an RNA guide sequence) or Neurospora VS RNA motif. Examples of hammerhead motifs are
 15 described by Rossi *et al.* (1992). Examples of hairpin motifs are described by Hampel *et al.* (Eur. Pat. Appl. Publ. No. EP 0360257), Hampel and Tritz (1989), Hampel *et al.* (1990) and U. S. Patent 5,631,359 (specifically incorporated herein by reference). An example of the hepatitis δ virus motif is described by Perrotta and Been (1992); an example of the RNaseP motif is described by Guerrier-Takada *et al.* (1983); Neurospora VS RNA
 20 ribozyme motif is described by Collins (Saville and Collins, 1990; Saville and Collins, 1991; Collins and Olive, 1993); and an example of the Group I intron is described in (U. S. Patent 4,987,071, specifically incorporated herein by reference). All that is important in an enzymatic nucleic acid molecule of this invention is that it has a specific substrate binding site which is complementary to one or more of the target gene RNA regions, and that it
 25 have nucleotide sequences within or surrounding that substrate binding site which impart an RNA cleaving activity to the molecule. Thus the ribozyme constructs need not be limited to specific motifs mentioned herein.

In certain embodiments, it may be important to produce enzymatic cleaving agents which exhibit a high degree of specificity for the RNA of a desired target, such as

one of the sequences disclosed herein. The enzymatic nucleic acid molecule is preferably targeted to a highly conserved sequence region of a target mRNA. Such enzymatic nucleic acid molecules can be delivered exogenously to specific cells as required. Alternatively, the ribozymes can be expressed from DNA or RNA vectors that are delivered to specific
 5 cells.

Small enzymatic nucleic acid motifs (*e.g.*, of the hammerhead or the hairpin structure) may also be used for exogenous delivery. The simple structure of these molecules increases the ability of the enzymatic nucleic acid to invade targeted regions of the mRNA structure. Alternatively, catalytic RNA molecules can be expressed within cells
 10 from eukaryotic promoters (*e.g.*, Scanlon *et al.*, 1991; Kashani-Sabet *et al.*, 1992; Dropulic *et al.*, 1992; Weerasinghe *et al.*, 1991; Ojwang *et al.*, 1992; Chen *et al.*, 1992; Sarver *et al.*, 1990). Those skilled in the art realize that any ribozyme can be expressed in eukaryotic cells from the appropriate DNA vector. The activity of such ribozymes can be augmented by their release from the primary transcript by a second ribozyme (Int. Pat. Appl. Publ. No.
 15 WO 93/23569, and Int. Pat. Appl. Publ. No. WO 94/02595, both hereby incorporated by reference; Ohkawa *et al.*, 1992; Taira *et al.*, 1991; and Ventura *et al.*, 1993).

Ribozymes may be added directly, or can be complexed with cationic lipids, lipid complexes, packaged within liposomes, or otherwise delivered to target cells. The RNA or RNA complexes can be locally administered to relevant tissues *ex vivo*, or *in vivo*
 20 through injection, aerosol inhalation, infusion pump or stent, with or without their incorporation in biopolymers.

Ribozymes may be designed as described in Int. Pat. Appl. Publ. No. WO 93/23569 and Int. Pat. Appl. Publ. No. WO 94/02595, each specifically incorporated herein by reference) and synthesized to be tested *in vitro* and *in vivo*, as described. Such
 25 ribozymes can also be optimized for delivery. While specific examples are provided, those in the art will recognize that equivalent RNA targets in other species can be utilized when necessary.

Hammerhead or hairpin ribozymes may be individually analyzed by computer folding (Jaeger *et al.*, 1989) to assess whether the ribozyme sequences fold into

the appropriate secondary structure. Those ribozymes with unfavorable intramolecular interactions between the binding arms and the catalytic core are eliminated from consideration. Varying binding arm lengths can be chosen to optimize activity. Generally, at least 5 or so bases on each arm are able to bind to, or otherwise interact with, the target

5 RNA.

Ribozymes of the hammerhead or hairpin motif may be designed to anneal to various sites in the mRNA message, and can be chemically synthesized. The method of synthesis used follows the procedure for normal RNA synthesis as described in Usman *et al.* (1987) and in Scaringe *et al.* (1990) and makes use of common nucleic acid

10 protecting and coupling groups, such as dimethoxytrityl at the 5'-end, and phosphoramidites at the 3'-end. Average stepwise coupling yields are typically >98%. Hairpin ribozymes may be synthesized in two parts and annealed to reconstruct an active ribozyme (Chowrira and Burke, 1992). Ribozymes may be modified extensively to enhance stability by modification with nuclease resistant groups, for example, 2'-amino, 2'-

15 C-allyl, 2'-fluoro, 2'-o-methyl, 2'-H (for a review see *e.g.*, Usman and Cedergren, 1992). Ribozymes may be purified by gel electrophoresis using general methods or by high pressure liquid chromatography and resuspended in water.

Ribozyme activity can be optimized by altering the length of the ribozyme binding arms, or chemically synthesizing ribozymes with modifications that prevent their

20 degradation by serum ribonucleases (see *e.g.*, Int. Pat. Appl. Publ. No. WO 92/07065; Perrault *et al.*, 1990; Pieken *et al.*, 1991; Usman and Cedergren, 1992; Int. Pat. Appl. Publ. No. WO 93/15187; Int. Pat. Appl. Publ. No. WO 91/03162; Eur. Pat. Appl. Publ. No. 92110298.4; U. S. Patent 5,334,711; and Int. Pat. Appl. Publ. No. WO 94/13688, which describe various chemical modifications that can be made to the sugar moieties of

25 enzymatic RNA molecules), modifications which enhance their efficacy in cells, and removal of stem II bases to shorten RNA synthesis times and reduce chemical requirements.

Sullivan *et al.* (Int. Pat. Appl. Publ. No. WO 94/02595) describes the general methods for delivery of enzymatic RNA molecules. Ribozymes may be

administered to cells by a variety of methods known to those familiar to the art, including, but not restricted to, encapsulation in liposomes, by iontophoresis, or by incorporation into other vehicles, such as hydrogels, cyclodextrins, biodegradable nanocapsules, and bioadhesive microspheres. For some indications, ribozymes may be directly delivered *ex vivo* to cells or tissues with or without the aforementioned vehicles. Alternatively, the RNA/vehicle combination may be locally delivered by direct inhalation, by direct injection or by use of a catheter, infusion pump or stent. Other routes of delivery include, but are not limited to, intravascular, intramuscular, subcutaneous or joint injection, aerosol inhalation, oral (tablet or pill form), topical, systemic, ocular, intraperitoneal and/or intrathecal delivery. More detailed descriptions of ribozyme delivery and administration are provided in Int. Pat. Appl. Publ. No. WO 94/02595 and Int. Pat. Appl. Publ. No. WO 93/23569, each specifically incorporated herein by reference.

Another means of accumulating high concentrations of a ribozyme(s) within cells is to incorporate the ribozyme-encoding sequences into a DNA expression vector. Transcription of the ribozyme sequences are driven from a promoter for eukaryotic RNA polymerase I (pol I), RNA polymerase II (pol II), or RNA polymerase III (pol III). Transcripts from pol II or pol III promoters will be expressed at high levels in all cells; the levels of a given pol II promoter in a given cell type will depend on the nature of the gene regulatory sequences (enhancers, silencers, *etc.*) present nearby. Prokaryotic RNA polymerase promoters may also be used, providing that the prokaryotic RNA polymerase enzyme is expressed in the appropriate cells (Elroy-Stein and Moss, 1990; Gao and Huang, 1993; Lieber *et al.*, 1993; Zhou *et al.*, 1990). Ribozymes expressed from such promoters can function in mammalian cells (*e.g.* Kashani-Saber *et al.*, 1992; Ojwang *et al.*, 1992; Chen *et al.*, 1992; Yu *et al.*, 1993; L'Huillier *et al.*, 1992; Lisiewicz *et al.*, 1993). Such transcription units can be incorporated into a variety of vectors for introduction into mammalian cells, including but not restricted to, plasmid DNA vectors, viral DNA vectors (such as adenovirus or adeno-associated vectors), or viral RNA vectors (such as retroviral, semliki forest virus, sindbis virus vectors).

Ribozymes may be used as diagnostic tools to examine genetic drift and mutations within diseased cells. They can also be used to assess levels of the target RNA molecule. The close relationship between ribozyme activity and the structure of the target RNA allows the detection of mutations in any region of the molecule which alters the base-pairing and three-dimensional structure of the target RNA. By using multiple ribozymes, one may map nucleotide changes which are important to RNA structure and function *in vitro*, as well as in cells and tissues. Cleavage of target RNAs with ribozymes may be used to inhibit gene expression and define the role (essentially) of specified gene products in the progression of disease. In this manner, other genetic targets may be defined as important mediators of the disease. These studies will lead to better treatment of the disease progression by affording the possibility of combinational therapies (*e.g.*, multiple ribozymes targeted to different genes, ribozymes coupled with known small molecule inhibitors, or intermittent treatment with combinations of ribozymes and/or other chemical or biological molecules). Other *in vitro* uses of ribozymes are well known in the art, and include detection of the presence of mRNA associated with an IL-5 related condition. Such RNA is detected by determining the presence of a cleavage product after treatment with a ribozyme using standard methodology.

PEPTIDE NUCLEIC ACIDS

In certain embodiments, the inventors contemplate the use of peptide nucleic acids (PNAs) in the practice of the methods of the invention. PNA is a DNA mimic in which the nucleobases are attached to a pseudopeptide backbone (Good and Nielsen, 1997). PNA is able to be utilized in a number methods that traditionally have used RNA or DNA. Often PNA sequences perform better in techniques than the corresponding RNA or DNA sequences and have utilities that are not inherent to RNA or DNA. A review of PNA including methods of making, characteristics of, and methods of using, is provided by Corey (1997) and is incorporated herein by reference. As such, in certain embodiments, one may prepare PNA sequences that are complementary to one or more portions of the ACE mRNA sequence, and such PNA compositions may be used to regulate, alter,

decrease, or reduce the translation of ACE-specific mRNA, and thereby alter the level of ACE activity in a host cell to which such PNA compositions have been administered.

PNAs have 2-aminoethyl-glycine linkages replacing the normal phosphodiester backbone of DNA (Nielsen *et al.*, 1991; Hanvey *et al.*, 1992; Hyrup and Nielsen, 1996; Neilsen, 1996). This chemistry has three important consequences: firstly, in contrast to DNA or phosphorothioate oligonucleotides, PNAs are neutral molecules; secondly, PNAs are achiral, which avoids the need to develop a stereoselective synthesis; and thirdly, PNA synthesis uses standard Boc (Dueholm *et al.*, 1994) or Fmoc (Thomson *et al.*, 1995) protocols for solid-phase peptide synthesis, although other methods, including a modified Merrifield method, have been used (Christensen *et al.*, 1995).

PNA monomers or ready-made oligomers are commercially available from PerSeptive Biosystems (Framingham, MA). PNA syntheses by either Boc or Fmoc protocols are straightforward using manual or automated protocols (Norton *et al.*, 1995). The manual protocol lends itself to the production of chemically modified PNAs or the simultaneous synthesis of families of closely related PNAs.

As with peptide synthesis, the success of a particular PNA synthesis will depend on the properties of the chosen sequence. For example, while in theory PNAs can incorporate any combination of nucleotide bases, the presence of adjacent purines can lead to deletions of one or more residues in the product. In expectation of this difficulty, it is suggested that, in producing PNAs with adjacent purines, one should repeat the coupling of residues likely to be added inefficiently. This should be followed by the purification of PNAs by reverse-phase high-pressure liquid chromatography (Norton *et al.*, 1995) providing yields and purity of product similar to those observed during the synthesis of peptides.

Modifications of PNAs for a given application may be accomplished by coupling amino acids during solid-phase synthesis or by attaching compounds that contain a carboxylic acid group to the exposed N-terminal amine. Alternatively, PNAs can be modified after synthesis by coupling to an introduced lysine or cysteine. The ease with which PNAs can be modified facilitates optimization for better solubility or for specific

functional requirements. Once synthesized, the identity of PNAs and their derivatives can be confirmed by mass spectrometry. Several studies have made and utilized modifications of PNAs (Norton *et al.*, 1995; Haaima *et al.*, 1996; Stetsenko *et al.*, 1996; Petersen *et al.*, 1995; Ulmann *et al.*, 1996; Koch *et al.*, 1995; Orum *et al.*, 1995; Footer *et al.*, 1996; 5 Griffith *et al.*, 1995; Kremsky *et al.*, 1996; Pardridge *et al.*, 1995; Boffa *et al.*, 1995; Landsdorp *et al.*, 1996; Gambacorti-Passerini *et al.*, 1996; Armitage *et al.*, 1997; Seeger *et al.*, 1997; Ruskowski *et al.*, 1997). U.S. Patent No. 5,700,922 discusses PNA-DNA-PNA chimeric molecules and their uses in diagnostics, modulating protein in organisms, and treatment of conditions susceptible to therapeutics.

10 In contrast to DNA and RNA, which contain negatively charged linkages, the PNA backbone is neutral. In spite of this dramatic alteration, PNAs recognize complementary DNA and RNA by Watson-Crick pairing (Egholm *et al.*, 1993), validating the initial modeling by Nielsen *et al.* (1991). PNAs lack 3' to 5' polarity and can bind in either parallel or antiparallel fashion, with the antiparallel mode being preferred (Egholm *et al.*, 1993). 15

Hybridization of DNA oligonucleotides to DNA and RNA is destabilized by electrostatic repulsion between the negatively charged phosphate backbones of the complementary strands. By contrast, the absence of charge repulsion in PNA-DNA or PNA-RNA duplexes increases the melting temperature (T_m) and reduces the dependence of 20 T_m on the concentration of mono- or divalent cations (Nielsen *et al.*, 1991). The enhanced rate and affinity of hybridization are significant because they are responsible for the surprising ability of PNAs to perform strand invasion of complementary sequences within relaxed double-stranded DNA. In addition, the efficient hybridization at inverted repeats suggests that PNAs can recognize secondary structure effectively within double-stranded 25 DNA. Enhanced recognition also occurs with PNAs immobilized on surfaces, and Wang *et al.* have shown that support-bound PNAs can be used to detect hybridization events (Wang *et al.*, 1996).

One might expect that tight binding of PNAs to complementary sequences would also increase binding to similar (but not identical) sequences, reducing the sequence

specificity of PNA recognition. As with DNA hybridization, however, selective recognition can be achieved by balancing oligomer length and incubation temperature. Moreover, selective hybridization of PNAs is encouraged by PNA-DNA hybridization being less tolerant of base mismatches than DNA-DNA hybridization. For example, a
 5 single mismatch within a 16 bp PNA-DNA duplex can reduce the T_m by up to 15°C (Egholm *et al.*, 1993). This high level of discrimination has allowed the development of several PNA-based strategies for the analysis of point mutations (Wang *et al.*, 1996; Carlsson *et al.*, 1996; Thiede *et al.*, 1996; Webb and Hurskainen, 1996; Perry-O'Keefe *et al.*, 1996).

10 High-affinity binding provides clear advantages for molecular recognition and the development of new applications for PNAs. For example, 11-13 nucleotide PNAs inhibit the activity of telomerase, a ribonucleo-protein that extends telomere ends using an essential RNA template, while the analogous DNA oligomers do not (Norton *et al.*, 1996).

Neutral PNAs are more hydrophobic than analogous DNA oligomers, and
 15 this can lead to difficulty solubilizing them at neutral pH, especially if the PNAs have a high purine content or if they have the potential to form secondary structures. Their solubility can be enhanced by attaching one or more positive charges to the PNA termini (Nielsen *et al.*, 1991).

Findings by Allfrey and colleagues suggest that strand invasion will occur
 20 spontaneously at sequences within chromosomal DNA (Boffa *et al.*, 1995; Boffa *et al.*, 1996). These studies targeted PNAs to triplet repeats of the nucleotides CAG and used this recognition to purify transcriptionally active DNA (Boffa *et al.*, 1995) and to inhibit transcription (Boffa *et al.*, 1996). This result suggests that if PNAs can be delivered within cells then they will have the potential to be general sequence-specific regulators of gene
 25 expression. Studies and reviews concerning the use of PNAs as antisense and anti-gene agents include Nielsen *et al.* (1993b), Hanvey *et al.* (1992), and Good and Nielsen (1997). Koppelhus *et al.* (1997) have used PNAs to inhibit HIV-1 inverse transcription, showing that PNAs may be used for antiviral therapies.

Methods of characterizing the antisense binding properties of PNAs are discussed in Rose (1993) and Jensen *et al.* (1997). Rose uses capillary gel electrophoresis to determine binding of PNAs to their complementary oligonucleotide, measuring the relative binding kinetics and stoichiometry. Similar types of measurements were made by

5 Jensen *et al.* using BIAcore™ technology.

Other applications of PNAs include use in DNA strand invasion (Nielsen *et al.*, 1991), antisense inhibition (Hanvey *et al.*, 1992), mutational analysis (Orum *et al.*, 1993), enhancers of transcription (Mollegaard *et al.*, 1994), nucleic acid purification (Orum *et al.*, 1995), isolation of transcriptionally active genes (Boffa *et al.*, 1995), blocking of

10 transcription factor binding (Vickers *et al.*, 1995), genome cleavage (Veselkov *et al.*, 1996), biosensors (Wang *et al.*, 1996), *in situ* hybridization (Thisted *et al.*, 1996), and in a alternative to Southern blotting (Perry-O'Keefe, 1996).

POLYPEPTIDE COMPOSITIONS

The present invention, in other aspects, provides polypeptide compositions.

15 Generally, a polypeptide of the invention will be an isolated polypeptide (or an epitope, variant, or active fragment thereof) derived from a mammalian species. Preferably, the polypeptide is encoded by a polynucleotide sequence disclosed herein or a sequence which hybridizes under moderately stringent conditions to a polynucleotide sequence disclosed herein. Alternatively, the polypeptide may be defined as a polypeptide which comprises a

20 contiguous amino acid sequence from an amino acid sequence disclosed herein, or which polypeptide comprises an entire amino acid sequence disclosed herein.

In the present invention, a polypeptide composition is also understood to comprise one or more polypeptides that are immunologically reactive with antibodies generated against a polypeptide of the invention, particularly a polypeptide having the

25 amino acid sequence disclosed in SEQ ID NO: 112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534, 537-551, 553-568, 573-586, 588-590, 592, 706-708, 775, 776, 778 and 780, or active fragments, variants or biological functional equivalents thereof.

Likewise, a polypeptide composition of the present invention is understood to comprise one or more polypeptides that are capable of eliciting antibodies that are immunologically reactive with one or more polypeptides encoded by one or more contiguous nucleic acid sequences contained in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823 and 824, or to active fragments, or to variants thereof, or to one or more nucleic acid sequences which hybridize to one or more of these sequences under conditions of moderate to high stringency. Particularly illustrative polypeptides include the amino acid sequence disclosed in SEQ ID NO: 112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534, 537-551, 553-568, 573-586, 588-590, 592, 706-708, 775, 776, 778 and 780.

As used herein, an active fragment of a polypeptide includes a whole or a portion of a polypeptide which is modified by conventional techniques, *e.g.*, mutagenesis, or by addition, deletion, or substitution, but which active fragment exhibits substantially the same structure function, antigenicity, etc., as a polypeptide as described herein.

In certain illustrative embodiments, the polypeptides of the invention will comprise at least an immunogenic portion of a prostate-specific protein or a variant thereof, as described herein. As noted above, a "prostate-specific protein" is a protein that is expressed by prostate cells. Proteins that are prostate-specific proteins also react detectably within an immunoassay (such as an ELISA) with antisera from a patient with prostate cancer. Polypeptides as described herein may be of any length. Additional sequences derived from the native protein and/or heterologous sequences may be present, and such sequences may (but need not) possess further immunogenic or antigenic properties.

An "immunogenic portion," as used herein is a portion of a protein that is recognized (*i.e.*, specifically bound) by a B-cell and/or T-cell surface antigen receptor. Such immunogenic portions generally comprise at least 5 amino acid residues, more preferably at least 10, and still more preferably at least 20 amino acid residues of a prostate-specific protein or a variant thereof. Certain preferred immunogenic portions

include peptides in which an N-terminal leader sequence and/or transmembrane domain have been deleted. Other preferred immunogenic portions may contain a small N- and/or C-terminal deletion (*e.g.*, 1-30 amino acids, preferably 5-15 amino acids), relative to the mature protein.

5 Immunogenic portions may generally be identified using well known techniques, such as those summarized in Paul, *Fundamental Immunology*, 3rd ed., 243-247 (Raven Press, 1993) and references cited therein. Such techniques include screening polypeptides for the ability to react with antigen-specific antibodies, antisera and/or T-cell lines or clones. As used herein, antisera and antibodies are "antigen-specific" if they
10 specifically bind to an antigen (*i.e.*, they react with the protein in an ELISA or other immunoassay, and do not react detectably with unrelated proteins). Such antisera and antibodies may be prepared as described herein, and using well known techniques. An immunogenic portion of a native prostate-specific protein is a portion that reacts with such antisera and/or T-cells at a level that is not substantially less than the reactivity of the full
15 length polypeptide (*e.g.*, in an ELISA and/or T-cell reactivity assay). Such immunogenic portions may react within such assays at a level that is similar to or greater than the reactivity of the full length polypeptide. Such screens may generally be performed using methods well known to those of ordinary skill in the art, such as those described in Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. For
20 example, a polypeptide may be immobilized on a solid support and contacted with patient sera to allow binding of antibodies within the sera to the immobilized polypeptide. Unbound sera may then be removed and bound antibodies detected using, for example, ¹²⁵I-labeled Protein A.

As noted above, a composition may comprise a variant of a native prostate-specific protein. A polypeptide "variant," as used herein, is a polypeptide that differs from
25 a native prostate-specific protein in one or more substitutions, deletions, additions and/or insertions, such that the immunogenicity of the polypeptide is not substantially diminished. In other words, the ability of a variant to react with antigen-specific antisera may be enhanced or unchanged, relative to the native protein, or may be diminished by less than

50%, and preferably less than 20%, relative to the native protein. Such variants may generally be identified by modifying one of the above polypeptide sequences and evaluating the reactivity of the modified polypeptide with antigen-specific antibodies or antisera as described herein. Preferred variants include those in which one or more
 5 portions, such as an N-terminal leader sequence or transmembrane domain, have been removed. Other preferred variants include variants in which a small portion (*e.g.*, 1-30 amino acids, preferably 5-15 amino acids) has been removed from the N- and/or C-terminal of the mature protein.

Polypeptide variants encompassed by the present invention include those
 10 exhibiting at least about 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% or more identity (determined as described above) to the polypeptides disclosed herein.

Preferably, a variant contains conservative substitutions. A "conservative substitution" is one in which an amino acid is substituted for another amino acid that has
 15 similar properties, such that one skilled in the art of peptide chemistry would expect the secondary structure and hydropathic nature of the polypeptide to be substantially unchanged. Amino acid substitutions may generally be made on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity and/or the amphipathic nature of the residues. For example, negatively charged amino acids include aspartic acid and
 20 glutamic acid; positively charged amino acids include lysine and arginine; and amino acids with uncharged polar head groups having similar hydrophilicity values include leucine, isoleucine and valine; glycine and alanine; asparagine and glutamine; and serine, threonine, phenylalanine and tyrosine. Other groups of amino acids that may represent conservative changes include: (1) ala, pro, gly, glu, asp, gln, asn, ser, thr; (2) cys, ser, tyr, thr; (3) val,
 25 ile, leu, met, ala, phe; (4) lys, arg, his; and (5) phe, tyr, trp, his. A variant may also, or alternatively, contain nonconservative changes. In a preferred embodiment, variant polypeptides differ from a native sequence by substitution, deletion or addition of five amino acids or fewer. Variants may also (or alternatively) be modified by, for example, the

deletion or addition of amino acids that have minimal influence on the immunogenicity, secondary structure and hydropathic nature of the polypeptide.

As noted above, polypeptides may comprise a signal (or leader) sequence at the N-terminal end of the protein, which co-translationally or post-translationally directs transfer of the protein. The polypeptide may also be conjugated to a linker or other sequence for ease of synthesis, purification or identification of the polypeptide (*e.g.*, poly-His), or to enhance binding of the polypeptide to a solid support. For example, a polypeptide may be conjugated to an immunoglobulin Fc region.

Polypeptides may be prepared using any of a variety of well known techniques. Recombinant polypeptides encoded by DNA sequences as described above may be readily prepared from the DNA sequences using any of a variety of expression vectors known to those of ordinary skill in the art. Expression may be achieved in any appropriate host cell that has been transformed or transfected with an expression vector containing a DNA molecule that encodes a recombinant polypeptide. Suitable host cells include prokaryotes, yeast, and higher eukaryotic cells, such as mammalian cells and plant cells. Preferably, the host cells employed are *E. coli*, yeast or a mammalian cell line such as COS or CHO. Supernatants from suitable host/vector systems which secrete recombinant protein or polypeptide into culture media may be first concentrated using a commercially available filter. Following concentration, the concentrate may be applied to a suitable purification matrix such as an affinity matrix or an ion exchange resin. Finally, one or more reverse phase HPLC steps can be employed to further purify a recombinant polypeptide.

Portions and other variants having less than about 100 amino acids, and generally less than about 50 amino acids, may also be generated by synthetic means, using techniques well known to those of ordinary skill in the art. For example, such polypeptides may be synthesized using any of the commercially available solid-phase techniques, such as the Merrifield solid-phase synthesis method, where amino acids are sequentially added to a growing amino acid chain. See Merrifield, *J. Am. Chem. Soc.* 85:2149-2146, 1963. Equipment for automated synthesis of polypeptides is commercially available from

suppliers such as Perkin Elmer/Applied BioSystems Division (Foster City, CA), and may be operated according to the manufacturer's instructions.

Within certain specific embodiments, a polypeptide may be a fusion protein that comprises multiple polypeptides as described herein, or that comprises at least one polypeptide as described herein and an unrelated sequence, such as a known tumor protein. A fusion partner may, for example, assist in providing T helper epitopes (an immunological fusion partner), preferably T helper epitopes recognized by humans, or may assist in expressing the protein (an expression enhancer) at higher yields than the native recombinant protein. Certain preferred fusion partners are both immunological and expression enhancing fusion partners. Other fusion partners may be selected so as to increase the solubility of the protein or to enable the protein to be targeted to desired intracellular compartments. Still further fusion partners include affinity tags, which facilitate purification of the protein.

Fusion proteins may generally be prepared using standard techniques, including chemical conjugation. Preferably, a fusion protein is expressed as a recombinant protein, allowing the production of increased levels, relative to a non-fused protein, in an expression system. Briefly, DNA sequences encoding the polypeptide components may be assembled separately, and ligated into an appropriate expression vector. The 3' end of the DNA sequence encoding one polypeptide component is ligated, with or without a peptide linker, to the 5' end of a DNA sequence encoding the second polypeptide component so that the reading frames of the sequences are in phase. This permits translation into a single fusion protein that retains the biological activity of both component polypeptides.

A peptide linker sequence may be employed to separate the first and second polypeptide components by a distance sufficient to ensure that each polypeptide folds into its secondary and tertiary structures. Such a peptide linker sequence is incorporated into the fusion protein using standard techniques well known in the art. Suitable peptide linker sequences may be chosen based on the following factors: (1) their ability to adopt a flexible extended conformation; (2) their inability to adopt a secondary structure that could interact with functional epitopes on the first and second polypeptides; and (3) the lack of

hydrophobic or charged residues that might react with the polypeptide functional epitopes. Preferred peptide linker sequences contain Gly, Asn and Ser residues. Other near neutral amino acids, such as Thr and Ala may also be used in the linker sequence. Amino acid sequences which may be usefully employed as linkers include those disclosed in Maratea *et al.*, *Gene* 40:39-46, 1985; Murphy *et al.*, *Proc. Natl. Acad. Sci. USA* 83:8258-8262, 1986; 5 U.S. Patent No. 4,935,233 and U.S. Patent No. 4,751,180. The linker sequence may generally be from 1 to about 50 amino acids in length. Linker sequences are not required when the first and second polypeptides have non-essential N-terminal amino acid regions that can be used to separate the functional domains and prevent steric interference.

10 The ligated DNA sequences are operably linked to suitable transcriptional or translational regulatory elements. The regulatory elements responsible for expression of DNA are located only 5' to the DNA sequence encoding the first polypeptides. Similarly, stop codons required to end translation and transcription termination signals are only present 3' to the DNA sequence encoding the second polypeptide.

15 Fusion proteins are also provided. Such proteins comprise a polypeptide as described herein together with an unrelated immunogenic protein. Preferably the immunogenic protein is capable of eliciting a recall response. Examples of such proteins include tetanus, tuberculosis and hepatitis proteins (*see*, for example, Stoute *et al.* *New Engl. J. Med.*, 336:86-91, 1997).

20 Within preferred embodiments, an immunological fusion partner is derived from protein D, a surface protein of the gram-negative bacterium Haemophilus influenza B (WO 91/18926). Preferably, a protein D derivative comprises approximately the first third of the protein (*e.g.*, the first N-terminal 100-110 amino acids), and a protein D derivative may be lipidated. Within certain preferred embodiments, the first 109 residues of a 25 Lipoprotein D fusion partner is included on the N-terminus to provide the polypeptide with additional exogenous T-cell epitopes and to increase the expression level in *E. coli* (thus functioning as an expression enhancer). The lipid tail ensures optimal presentation of the antigen to antigen presenting cells. Other fusion partners include the non-structural protein

from influenzae virus, NS1 (hemagglutinin). Typically, the N-terminal 81 amino acids are used, although different fragments that include T-helper epitopes may be used.

In another embodiment, the immunological fusion partner is the protein known as LYTA, or a portion thereof (preferably a C-terminal portion). LYTA is derived from *Streptococcus pneumoniae*, which synthesizes an N-acetyl-L-alanine amidase known as amidase LYTA (encoded by the *LytA* gene; *Gene* 43:265-292, 1986). LYTA is an autolysin that specifically degrades certain bonds in the peptidoglycan backbone. The C-terminal domain of the LYTA protein is responsible for the affinity to the choline or to some choline analogues such as DEAE. This property has been exploited for the development of *E. coli* C-LYTA expressing plasmids useful for expression of fusion proteins. Purification of hybrid proteins containing the C-LYTA fragment at the amino terminus has been described (*see Biotechnology* 10:795-798, 1992). Within a preferred embodiment, a repeat portion of LYTA may be incorporated into a fusion protein. A repeat portion is found in the C-terminal region starting at residue 178. A particularly preferred repeat portion incorporates residues 188-305.

In general, polypeptides (including fusion proteins) and polynucleotides as described herein are isolated. An "isolated" polypeptide or polynucleotide is one that is removed from its original environment. For example, a naturally-occurring protein is isolated if it is separated from some or all of the coexisting materials in the natural system. Preferably, such polypeptides are at least about 90% pure, more preferably at least about 95% pure and most preferably at least about 99% pure. A polynucleotide is considered to be isolated if, for example, it is cloned into a vector that is not a part of the natural environment.

BINDING AGENTS

The present invention further provides agents, such as antibodies and antigen-binding fragments thereof, that specifically bind to a prostate-specific protein. As used herein, an antibody, or antigen-binding fragment thereof, is said to "specifically bind" to a prostate-specific protein if it reacts at a detectable level (within, for example, an

ELISA) with a prostate-specific protein, and does not react detectably with unrelated proteins under similar conditions. As used herein, "binding" refers to a noncovalent association between two separate molecules such that a complex is formed. The ability to bind may be evaluated by, for example, determining a binding constant for the formation of the complex. The binding constant is the value obtained when the concentration of the complex is divided by the product of the component concentrations. In general, two compounds are said to "bind," in the context of the present invention, when the binding constant for complex formation exceeds about 10^3 L/mol. The binding constant may be determined using methods well known in the art.

Binding agents may be further capable of differentiating between patients with and without a cancer, such as prostate cancer, using the representative assays provided herein. In other words, antibodies or other binding agents that bind to a prostate-specific protein will generate a signal indicating the presence of a cancer in at least about 20% of patients with the disease, and will generate a negative signal indicating the absence of the disease in at least about 90% of individuals without the cancer. To determine whether a binding agent satisfies this requirement, biological samples (*e.g.*, blood, sera, sputum, urine and/or tumor biopsies) from patients with and without a cancer (as determined using standard clinical tests) may be assayed as described herein for the presence of polypeptides that bind to the binding agent. It will be apparent that a statistically significant number of samples with and without the disease should be assayed. Each binding agent should satisfy the above criteria; however, those of ordinary skill in the art will recognize that binding agents may be used in combination to improve sensitivity.

Any agent that satisfies the above requirements may be a binding agent. For example, a binding agent may be a ribosome, with or without a peptide component, an RNA molecule or a polypeptide. In a preferred embodiment, a binding agent is an antibody or an antigen-binding fragment thereof. Antibodies may be prepared by any of a variety of techniques known to those of ordinary skill in the art. *See, e.g.*, Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In general, antibodies can be produced by cell culture techniques, including the generation of

monoclonal antibodies as described herein, or via transfection of antibody genes into suitable bacterial or mammalian cell hosts, in order to allow for the production of recombinant antibodies. In one technique, an immunogen comprising the polypeptide is initially injected into any of a wide variety of mammals (*e.g.*, mice, rats, rabbits, sheep or goats). In this step, the polypeptides of this invention may serve as the immunogen without modification. Alternatively, particularly for relatively short polypeptides, a superior immune response may be elicited if the polypeptide is joined to a carrier protein, such as bovine serum albumin or keyhole limpet hemocyanin. The immunogen is injected into the animal host, preferably according to a predetermined schedule incorporating one or more booster immunizations, and the animals are bled periodically. Polyclonal antibodies specific for the polypeptide may then be purified from such antisera by, for example, affinity chromatography using the polypeptide coupled to a suitable solid support.

Monoclonal antibodies specific for an antigenic polypeptide of interest may be prepared, for example, using the technique of Kohler and Milstein, *Eur. J. Immunol.* 6:511-519, 1976, and improvements thereto. Briefly, these methods involve the preparation of immortal cell lines capable of producing antibodies having the desired specificity (*i.e.*, reactivity with the polypeptide of interest). Such cell lines may be produced, for example, from spleen cells obtained from an animal immunized as described above. The spleen cells are then immortalized by, for example, fusion with a myeloma cell fusion partner, preferably one that is syngeneic with the immunized animal. A variety of fusion techniques may be employed. For example, the spleen cells and myeloma cells may be combined with a nonionic detergent for a few minutes and then plated at low density on a selective medium that supports the growth of hybrid cells, but not myeloma cells. A preferred selection technique uses HAT (hypoxanthine, aminopterin, thymidine) selection. After a sufficient time, usually about 1 to 2 weeks, colonies of hybrids are observed. Single colonies are selected and their culture supernatants tested for binding activity against the polypeptide. Hybridomas having high reactivity and specificity are preferred.

Monoclonal antibodies may be isolated from the supernatants of growing hybridoma colonies. In addition, various techniques may be employed to enhance the

yield, such as injection of the hybridoma cell line into the peritoneal cavity of a suitable vertebrate host, such as a mouse. Monoclonal antibodies may then be harvested from the ascites fluid or the blood. Contaminants may be removed from the antibodies by conventional techniques, such as chromatography, gel filtration, precipitation, and
 5 extraction. The polypeptides of this invention may be used in the purification process in, for example, an affinity chromatography step.

Within certain embodiments, the use of antigen-binding fragments of antibodies may be preferred. Such fragments include Fab fragments, which may be prepared using standard techniques. Briefly, immunoglobulins may be purified from rabbit
 10 serum by affinity chromatography on Protein A bead columns (Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988) and digested by papain to yield Fab and Fc fragments. The Fab and Fc fragments may be separated by affinity chromatography on protein A bead columns.

Monoclonal antibodies of the present invention may be coupled to one or
 15 more therapeutic agents. Suitable agents in this regard include radionuclides, differentiation inducers, drugs, toxins, and derivatives thereof. Preferred radionuclides include ^{90}Y , ^{123}I , ^{125}I , ^{131}I , ^{186}Re , ^{188}Re , ^{211}At , and ^{212}Bi . Preferred drugs include methotrexate, and pyrimidine and purine analogs. Preferred differentiation inducers include phorbol esters and butyric acid. Preferred toxins include ricin, abrin, diphtheria
 20 toxin, cholera toxin, gelonin, *Pseudomonas* exotoxin, *Shigella* toxin, and pokeweed antiviral protein.

A therapeutic agent may be coupled (*e.g.*, covalently bonded) to a suitable monoclonal antibody either directly or indirectly (*e.g.*, via a linker group). A direct reaction between an agent and an antibody is possible when each possesses a substituent
 25 capable of reacting with the other. For example, a nucleophilic group, such as an amino or sulfhydryl group, on one may be capable of reacting with a carbonyl-containing group, such as an anhydride or an acid halide, or with an alkyl group containing a good leaving group (*e.g.*, a halide) on the other.

Alternatively, it may be desirable to couple a therapeutic agent and an antibody via a linker group. A linker group can function as a spacer to distance an antibody from an agent in order to avoid interference with binding capabilities. A linker group can also serve to increase the chemical reactivity of a substituent on an agent or an antibody, and thus increase the coupling efficiency. An increase in chemical reactivity may also facilitate the use of agents, or functional groups on agents, which otherwise would not be possible.

It will be evident to those skilled in the art that a variety of bifunctional or polyfunctional reagents, both homo- and hetero-functional (such as those described in the catalog of the Pierce Chemical Co., Rockford, IL), may be employed as the linker group. Coupling may be effected, for example, through amino groups, carboxyl groups, sulfhydryl groups or oxidized carbohydrate residues. There are numerous references describing such methodology, *e.g.*, U.S. Patent No. 4,671,958, to Rodwell *et al.*

Where a therapeutic agent is more potent when free from the antibody portion of the immunoconjugates of the present invention, it may be desirable to use a linker group which is cleavable during or upon internalization into a cell. A number of different cleavable linker groups have been described. The mechanisms for the intracellular release of an agent from these linker groups include cleavage by reduction of a disulfide bond (*e.g.*, U.S. Patent No. 4,489,710, to Spitler), by irradiation of a photolabile bond (*e.g.*, U.S. Patent No. 4,625,014, to Senter *et al.*), by hydrolysis of derivatized amino acid side chains (*e.g.*, U.S. Patent No. 4,638,045, to Kohn *et al.*), by serum complement-mediated hydrolysis (*e.g.*, U.S. Patent No. 4,671,958, to Rodwell *et al.*), and acid-catalyzed hydrolysis (*e.g.*, U.S. Patent No. 4,569,789, to Blattler *et al.*).

It may be desirable to couple more than one agent to an antibody. In one embodiment, multiple molecules of an agent are coupled to one antibody molecule. In another embodiment, more than one type of agent may be coupled to one antibody. Regardless of the particular embodiment, immunoconjugates with more than one agent may be prepared in a variety of ways. For example, more than one agent may be coupled

directly to an antibody molecule, or linkers that provide multiple sites for attachment can be used. Alternatively, a carrier can be used.

A carrier may bear the agents in a variety of ways, including covalent bonding either directly or via a linker group. Suitable carriers include proteins such as albumins (*e.g.*, U.S. Patent No. 4,507,234, to Kato *et al.*), peptides and polysaccharides such as aminodextran (*e.g.*, U.S. Patent No. 4,699,784, to Shih *et al.*). A carrier may also bear an agent by noncovalent bonding or by encapsulation, such as within a liposome vesicle (*e.g.*, U.S. Patent Nos. 4,429,008 and 4,873,088). Carriers specific for radionuclide agents include radiohalogenated small molecules and chelating compounds. For example, U.S. Patent No. 4,735,792 discloses representative radiohalogenated small molecules and their synthesis. A radionuclide chelate may be formed from chelating compounds that include those containing nitrogen and sulfur atoms as the donor atoms for binding the metal, or metal oxide, radionuclide. For example, U.S. Patent No. 4,673,562, to Davison *et al.* discloses representative chelating compounds and their synthesis.

A variety of routes of administration for the antibodies and immunoconjugates may be used. Typically, administration will be intravenous, intramuscular, subcutaneous or in the bed of a resected tumor. It will be evident that the precise dose of the antibody/immunoconjugate will vary depending upon the antibody used, the antigen density on the tumor, and the rate of clearance of the antibody.

20 T CELLS

Immunotherapeutic compositions may also, or alternatively, comprise T cells specific for a prostate-specific protein. Such cells may generally be prepared *in vitro* or *ex vivo*, using standard procedures. For example, T cells may be isolated from bone marrow, peripheral blood, or a fraction of bone marrow or peripheral blood of a patient, using a commercially available cell separation system, such as the Isolex™ System, available from Nexell Therapeutics, Inc. (Irvine, CA; see also U.S. Patent No. 5,240,856; U.S. Patent No. 5,215,926; WO 89/06280; WO 91/16116 and WO 92/07243).

Alternatively, T cells may be derived from related or unrelated humans, non-human mammals, cell lines or cultures.

T cells may be stimulated with a prostate-specific polypeptide, polynucleotide encoding a prostate-specific polypeptide and/or an antigen presenting cell (APC) that expresses such a polypeptide. Such stimulation is performed under conditions and for a time sufficient to permit the generation of T cells that are specific for the polypeptide. Preferably, a prostate-specific polypeptide or polynucleotide is present within a delivery vehicle, such as a microsphere, to facilitate the generation of specific T cells.

T cells are considered to be specific for a prostate-specific polypeptide if the T cells specifically proliferate, secrete cytokines or kill target cells coated with the polypeptide or expressing a gene encoding the polypeptide. T cell specificity may be evaluated using any of a variety of standard techniques. For example, within a chromium release assay or proliferation assay, a stimulation index of more than two fold increase in lysis and/or proliferation, compared to negative controls, indicates T cell specificity. Such assays may be performed, for example, as described in Chen *et al.*, *Cancer Res.* 54:1065-1070, 1994. Alternatively, detection of the proliferation of T cells may be accomplished by a variety of known techniques. For example, T cell proliferation can be detected by measuring an increased rate of DNA synthesis (*e.g.*, by pulse-labeling cultures of T cells with tritiated thymidine and measuring the amount of tritiated thymidine incorporated into DNA). Contact with a prostate-specific polypeptide (100 ng/ml - 100 µg/ml, preferably 200 ng/ml - 25 µg/ml) for 3 - 7 days should result in at least a two fold increase in proliferation of the T cells. Contact as described above for 2-3 hours should result in activation of the T cells, as measured using standard cytokine assays in which a two fold increase in the level of cytokine release (*e.g.*, TNF or IFN-γ) is indicative of T cell activation (*see* Coligan *et al.*, *Current Protocols in Immunology*, vol. 1, Wiley Interscience (Greene 1998)). T cells that have been activated in response to a prostate-specific polypeptide, polynucleotide or polypeptide-expressing APC may be CD4⁺ and/or CD8⁺. prostate-specific protein-specific T cells may be expanded using standard techniques.

Within preferred embodiments, the T cells are derived from a patient, a related donor or an unrelated donor, and are administered to the patient following stimulation and expansion.

For therapeutic purposes, CD4⁺ or CD8⁺ T cells that proliferate in response to a prostate-specific polypeptide, polynucleotide or APC can be expanded in number either *in vitro* or *in vivo*. Proliferation of such T cells *in vitro* may be accomplished in a variety of ways. For example, the T cells can be re-exposed to a prostate-specific polypeptide, or a short peptide corresponding to an immunogenic portion of such a polypeptide, with or without the addition of T cell growth factors, such as interleukin-2, and/or stimulator cells that synthesize a prostate-specific polypeptide. Alternatively, one or more T cells that proliferate in the presence of a prostate-specific protein can be expanded in number by cloning. Methods for cloning cells are well known in the art, and include limiting dilution.

PHARMACEUTICAL COMPOSITIONS

In additional embodiments, the present invention concerns formulation of one or more of the polynucleotide, polypeptide, T-cell and/or antibody compositions disclosed herein in pharmaceutically-acceptable solutions for administration to a cell or an animal, either alone, or in combination with one or more other modalities of therapy.

It will also be understood that, if desired, the nucleic acid segment, RNA, DNA or PNA compositions that express a polypeptide as disclosed herein may be administered in combination with other agents as well, such as, *e.g.*, other proteins or polypeptides or various pharmaceutically-active agents. In fact, there is virtually no limit to other components that may also be included, given that the additional agents do not cause a significant adverse effect upon contact with the target cells or host tissues. The compositions may thus be delivered along with various other agents as required in the particular instance. Such compositions may be purified from host cells or other biological sources, or alternatively may be chemically synthesized as described herein. Likewise, such compositions may further comprise substituted or derivatized RNA or DNA compositions.

Formulation of pharmaceutically-acceptable excipients and carrier solutions is well-known to those of skill in the art, as is the development of suitable dosing and treatment regimens for using the particular compositions described herein in a variety of treatment regimens, including *e.g.*, oral, parenteral, intravenous, intranasal, and
 5 intramuscular administration and formulation.

1. ORAL DELIVERY

In certain applications, the pharmaceutical compositions disclosed herein may be delivered *via* oral administration to an animal. As such, these compositions may be formulated with an inert diluent or with an assimilable edible carrier, or they may be
 10 enclosed in hard- or soft-shell gelatin capsule, or they may be compressed into tablets, or they may be incorporated directly with the food of the diet.

The active compounds may even be incorporated with excipients and used in the form of ingestible tablets, buccal tables, troches, capsules, elixirs, suspensions, syrups, wafers, and the like (Mathiowitz *et al.*, 1997; Hwang *et al.*, 1998; U. S. Patent
 15 5,641,515; U. S. Patent 5,580,579 and U. S. Patent 5,792,451, each specifically incorporated herein by reference in its entirety). The tablets, troches, pills, capsules and the like may also contain the following: a binder, as gum tragacanth, acacia, cornstarch, or gelatin; excipients, such as dicalcium phosphate; a disintegrating agent, such as corn starch, potato starch, alginic acid and the like; a lubricant, such as magnesium stearate; and a
 20 sweetening agent, such as sucrose, lactose or saccharin may be added or a flavoring agent, such as peppermint, oil of wintergreen, or cherry flavoring. When the dosage unit form is a capsule, it may contain, in addition to materials of the above type, a liquid carrier. Various other materials may be present as coatings or to otherwise modify the physical form of the dosage unit. For instance, tablets, pills, or capsules may be coated with shellac, sugar, or
 25 both. A syrup of elixir may contain the active compound sucrose as a sweetening agent methyl and propylparabens as preservatives, a dye and flavoring, such as cherry or orange flavor. Of course, any material used in preparing any dosage unit form should be pharmaceutically pure and substantially non-toxic in the amounts employed. In addition,

the active compounds may be incorporated into sustained-release preparation and formulations.

Typically, these formulations may contain at least about 0.1% of the active compound or more, although the percentage of the active ingredient(s) may, of course, be varied and may conveniently be between about 1 or 2% and about 60% or 70% or more of the weight or volume of the total formulation. Naturally, the amount of active compound(s) in each therapeutically useful composition may be prepared in such a way that a suitable dosage will be obtained in any given unit dose of the compound. Factors such as solubility, bioavailability, biological half-life, route of administration, product shelf life, as well as other pharmacological considerations will be contemplated by one skilled in the art of preparing such pharmaceutical formulations, and as such, a variety of dosages and treatment regimens may be desirable.

For oral administration the compositions of the present invention may alternatively be incorporated with one or more excipients in the form of a mouthwash, dentifrice, buccal tablet, oral spray, or sublingual orally-administered formulation. For example, a mouthwash may be prepared incorporating the active ingredient in the required amount in an appropriate solvent, such as a sodium borate solution (Dobell's Solution). Alternatively, the active ingredient may be incorporated into an oral solution such as one containing sodium borate, glycerin and potassium bicarbonate, or dispersed in a dentifrice, or added in a therapeutically-effective amount to a composition that may include water, binders, abrasives, flavoring agents, foaming agents, and humectants. Alternatively the compositions may be fashioned into a tablet or solution form that may be placed under the tongue or otherwise dissolved in the mouth.

2. INJECTABLE DELIVERY

In certain circumstances it will be desirable to deliver the pharmaceutical compositions disclosed herein parenterally, intravenously, intramuscularly, or even intraperitoneally as described in U. S. Patent 5,543,158; U. S. Patent 5,641,515 and U. S. Patent 5,399,363 (each specifically incorporated herein by reference in its entirety).

Solutions of the active compounds as free base or pharmacologically acceptable salts may be prepared in water suitably mixed with a surfactant, such as hydroxypropylcellulose. Dispersions may also be prepared in glycerol, liquid polyethylene glycols, and mixtures thereof and in oils. Under ordinary conditions of storage and use, these preparations
 5 contain a preservative to prevent the growth of microorganisms.

The pharmaceutical forms suitable for injectable use include sterile aqueous solutions or dispersions and sterile powders for the extemporaneous preparation of sterile injectable solutions or dispersions (U. S. Patent 5,466,468, specifically incorporated herein by reference in its entirety). In all cases the form must be sterile and must be fluid to the
 10 extent that easy syringability exists. It must be stable under the conditions of manufacture and storage and must be preserved against the contaminating action of microorganisms, such as bacteria and fungi. The carrier can be a solvent or dispersion medium containing, for example, water, ethanol, polyol (*e.g.*, glycerol, propylene glycol, and liquid polyethylene glycol, and the like), suitable mixtures thereof, and/or vegetable oils. Proper
 15 fluidity may be maintained, for example, by the use of a coating, such as lecithin, by the maintenance of the required particle size in the case of dispersion and by the use of surfactants. The prevention of the action of microorganisms can be facilitated by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, sorbic acid, thimerosal, and the like. In many cases, it will be preferable to include isotonic agents, for example, sugars or sodium chloride. Prolonged absorption of the injectable
 20 compositions can be brought about by the use in the compositions of agents delaying absorption, for example, aluminum monostearate and gelatin.

For parenteral administration in an aqueous solution, for example, the solution should be suitably buffered if necessary and the liquid diluent first rendered
 25 isotonic with sufficient saline or glucose. These particular aqueous solutions are especially suitable for intravenous, intramuscular, subcutaneous and intraperitoneal administration. In this connection, a sterile aqueous medium that can be employed will be known to those of skill in the art in light of the present disclosure. For example, one dosage may be dissolved in 1 ml of isotonic NaCl solution and either added to 1000 ml of hypodermoclysis fluid or

injected at the proposed site of infusion, (see for example, "Remington's Pharmaceutical Sciences" 15th Edition, pages 1035-1038 and 1570-1580). Some variation in dosage will necessarily occur depending on the condition of the subject being treated. The person responsible for administration will, in any event, determine the appropriate dose for the individual subject. Moreover, for human administration, preparations should meet sterility, pyrogenicity, and the general safety and purity standards as required by FDA Office of Biologics standards.

Sterile injectable solutions are prepared by incorporating the active compounds in the required amount in the appropriate solvent with various of the other ingredients enumerated above, as required, followed by filtered sterilization. Generally, dispersions are prepared by incorporating the various sterilized active ingredients into a sterile vehicle which contains the basic dispersion medium and the required other ingredients from those enumerated above. In the case of sterile powders for the preparation of sterile injectable solutions, the preferred methods of preparation are vacuum-drying and freeze-drying techniques which yield a powder of the active ingredient plus any additional desired ingredient from a previously sterile-filtered solution thereof.

The compositions disclosed herein may be formulated in a neutral or salt form. Pharmaceutically-acceptable salts, include the acid addition salts (formed with the free amino groups of the protein) and which are formed with inorganic acids such as, for example, hydrochloric or phosphoric acids, or such organic acids as acetic, oxalic, tartaric, mandelic, and the like. Salts formed with the free carboxyl groups can also be derived from inorganic bases such as, for example, sodium, potassium, ammonium, calcium, or ferric hydroxides, and such organic bases as isopropylamine, trimethylamine, histidine, procaine and the like. Upon formulation, solutions will be administered in a manner compatible with the dosage formulation and in such amount as is therapeutically effective. The formulations are easily administered in a variety of dosage forms such as injectable solutions, drug-release capsules, and the like.

As used herein, "carrier" includes any and all solvents, dispersion media, vehicles, coatings, diluents, antibacterial and antifungal agents, isotonic and absorption

delaying agents, buffers, carrier solutions, suspensions, colloids, and the like. The use of such media and agents for pharmaceutical active substances is well known in the art. Except insofar as any conventional media or agent is incompatible with the active ingredient, its use in the therapeutic compositions is contemplated. Supplementary active
 5 ingredients can also be incorporated into the compositions.

The phrase "pharmaceutically-acceptable" refers to molecular entities and compositions that do not produce an allergic or similar untoward reaction when administered to a human. The preparation of an aqueous composition that contains a protein as an active ingredient is well understood in the art. Typically, such compositions
 10 are prepared as injectables, either as liquid solutions or suspensions; solid forms suitable for solution in, or suspension in, liquid prior to injection can also be prepared. The preparation can also be emulsified.

3. NASAL DELIVERY

In certain embodiments, the pharmaceutical compositions may be delivered
 15 by intranasal sprays, inhalation, and/or other aerosol delivery vehicles. Methods for delivering genes, nucleic acids, and peptide compositions directly to the lungs *via* nasal aerosol sprays has been described *e.g.*, in U. S. Patent 5,756,353 and U. S. Patent 5,804,212 (each specifically incorporated herein by reference in its entirety). Likewise, the delivery of drugs using intranasal microparticle resins (Takenaga *et al.*, 1998) and lysophosphatidyl-
 20 glycerol compounds (U. S. Patent 5,725,871, specifically incorporated herein by reference in its entirety) are also well-known in the pharmaceutical arts. Likewise, transmucosal drug delivery in the form of a polytetrafluoroethylene support matrix is described in U. S. Patent 5,780,045 (specifically incorporated herein by reference in its entirety).

4. LIPOSOME-, NANOCAPSULE-, AND MICROPARTICLE-MEDIATED DELIVERY

25 In certain embodiments, the inventors contemplate the use of liposomes, nanocapsules, microparticles, microspheres, lipid particles, vesicles, and the like, for the introduction of the compositions of the present invention into suitable host cells. In

particular, the compositions of the present invention may be formulated for delivery either encapsulated in a lipid particle, a liposome, a vesicle, a nanosphere, or a nanoparticle or the like.

Such formulations may be preferred for the introduction of
 5 pharmaceutically-acceptable formulations of the nucleic acids or constructs disclosed herein. The formation and use of liposomes is generally known to those of skill in the art (see for example, Couvreur *et al.*, 1977; Couvreur, 1988; Lasic, 1998; which describes the use of liposomes and nanocapsules in the targeted antibiotic therapy for intracellular bacterial infections and diseases). Recently, liposomes were developed with improved
 10 serum stability and circulation half-times (Gabizon and Papahadjopoulos, 1988; Allen and Choun, 1987; U. S. Patent 5,741,516, specifically incorporated herein by reference in its entirety). Further, various methods of liposome and liposome like preparations as potential drug carriers have been reviewed (Takakura, 1998; Chandran *et al.*, 1997; Margalit, 1995; U. S. Patent 5,567,434; U. S. Patent 5,552,157; U. S. Patent 5,565,213; U. S. Patent
 15 5,738,868 and U. S. Patent 5,795,587, each specifically incorporated herein by reference in its entirety).

Liposomes have been used successfully with a number of cell types that are normally resistant to transfection by other procedures including T cell suspensions, primary hepatocyte cultures and PC 12 cells (Renneisen *et al.*, 1990; Muller *et al.*, 1990). In
 20 addition, liposomes are free of the DNA length constraints that are typical of viral-based delivery systems. Liposomes have been used effectively to introduce genes, drugs (Heath and Martin, 1986; Heath *et al.*, 1986; Balazsovits *et al.*, 1989; Fresta and Puglisi, 1996), radiotherapeutic agents (Pikul *et al.*, 1987), enzymes (Imaizumi *et al.*, 1990a; Imaizumi *et al.*, 1990b), viruses (Faller and Baltimore, 1984), transcription factors and allosteric
 25 effectors (Nicolau and Gersonde, 1979) into a variety of cultured cell lines and animals. In addition, several successful clinical trails examining the effectiveness of liposome-mediated drug delivery have been completed (Lopez-Berestein *et al.*, 1985a; 1985b; Coune, 1988; Sculier *et al.*, 1988). Furthermore, several studies suggest that the use of

liposomes is not associated with autoimmune responses, toxicity or gonadal localization after systemic delivery (Mori and Fukatsu, 1992).

Liposomes are formed from phospholipids that are dispersed in an aqueous medium and spontaneously form multilamellar concentric bilayer vesicles (also termed multilamellar vesicles (MLVs)). MLVs generally have diameters of from 25 nm to 4 μ m. Sonication of MLVs results in the formation of small unilamellar vesicles (SUVs) with diameters in the range of 200 to 500 Å, containing an aqueous solution in the core.

Liposomes bear resemblance to cellular membranes and are contemplated for use in connection with the present invention as carriers for the peptide compositions. They are widely suitable as both water- and lipid-soluble substances can be entrapped, *i.e.* in the aqueous spaces and within the bilayer itself, respectively. It is possible that the drug-bearing liposomes may even be employed for site-specific delivery of active agents by selectively modifying the liposomal formulation.

In addition to the teachings of Couvreur *et al.* (1977; 1988), the following information may be utilized in generating liposomal formulations. Phospholipids can form a variety of structures other than liposomes when dispersed in water, depending on the molar ratio of lipid to water. At low ratios the liposome is the preferred structure. The physical characteristics of liposomes depend on pH, ionic strength and the presence of divalent cations. Liposomes can show low permeability to ionic and polar substances, but at elevated temperatures undergo a phase transition which markedly alters their permeability. The phase transition involves a change from a closely packed, ordered structure, known as the gel state, to a loosely packed, less-ordered structure, known as the fluid state. This occurs at a characteristic phase-transition temperature and results in an increase in permeability to ions, sugars and drugs.

In addition to temperature, exposure to proteins can alter the permeability of liposomes. Certain soluble proteins, such as cytochrome c, bind, deform and penetrate the bilayer, thereby causing changes in permeability. Cholesterol inhibits this penetration of proteins, apparently by packing the phospholipids more tightly. It is contemplated that the

most useful liposome formations for antibiotic and inhibitor delivery will contain cholesterol.

The ability to trap solutes varies between different types of liposomes. For example, MLVs are moderately efficient at trapping solutes, but SUVs are extremely inefficient. SUVs offer the advantage of homogeneity and reproducibility in size distribution, however, and a compromise between size and trapping efficiency is offered by large unilamellar vesicles (LUVs). These are prepared by ether evaporation and are three to four times more efficient at solute entrapment than MLVs.

In addition to liposome characteristics, an important determinant in entrapping compounds is the physicochemical properties of the compound itself. Polar compounds are trapped in the aqueous spaces and nonpolar compounds bind to the lipid bilayer of the vesicle. Polar compounds are released through permeation or when the bilayer is broken, but nonpolar compounds remain affiliated with the bilayer unless it is disrupted by temperature or exposure to lipoproteins. Both types show maximum efflux rates at the phase transition temperature.

Liposomes interact with cells *via* four different mechanisms: endocytosis by phagocytic cells of the reticuloendothelial system such as macrophages and neutrophils; adsorption to the cell surface, either by nonspecific weak hydrophobic or electrostatic forces, or by specific interactions with cell-surface components; fusion with the plasma cell membrane by insertion of the lipid bilayer of the liposome into the plasma membrane, with simultaneous release of liposomal contents into the cytoplasm; and by transfer of liposomal lipids to cellular or subcellular membranes, or vice versa, without any association of the liposome contents. It often is difficult to determine which mechanism is operative and more than one may operate at the same time.

The fate and disposition of intravenously injected liposomes depend on their physical properties, such as size, fluidity, and surface charge. They may persist in tissues for h or days, depending on their composition, and half lives in the blood range from min to several h. Larger liposomes, such as MLVs and LUVs, are taken up rapidly by phagocytic cells of the reticuloendothelial system, but physiology of the circulatory system restrains

the exit of such large species at most sites. They can exit only in places where large openings or pores exist in the capillary endothelium, such as the sinusoids of the liver or spleen. Thus, these organs are the predominate site of uptake. On the other hand, SUVs show a broader tissue distribution but still are sequestered highly in the liver and spleen. In
 5 general, this *in vivo* behavior limits the potential targeting of liposomes to only those organs and tissues accessible to their large size. These include the blood, liver, spleen, bone marrow, and lymphoid organs.

Targeting is generally not a limitation in terms of the present invention. However, should specific targeting be desired, methods are available for this to be
 10 accomplished. Antibodies may be used to bind to the liposome surface and to direct the antibody and its drug contents to specific antigenic receptors located on a particular cell-type surface. Carbohydrate determinants (glycoprotein or glycolipid cell-surface components that play a role in cell-cell recognition, interaction and adhesion) may also be used as recognition sites as they have potential in directing liposomes to particular cell
 15 types. Mostly, it is contemplated that intravenous injection of liposomal preparations would be used, but other routes of administration are also conceivable.

Alternatively, the invention provides for pharmaceutically-acceptable nanocapsule formulations of the compositions of the present invention. Nanocapsules can generally entrap compounds in a stable and reproducible way (Henry-Michelland *et al.*,
 20 1987; Quintanar-Guerrero *et al.*, 1998; Douglas *et al.*, 1987). To avoid side effects due to intracellular polymeric overloading, such ultrafine particles (sized around 0.1 μm) should be designed using polymers able to be degraded *in vivo*. Biodegradable polyalkylcyanoacrylate nanoparticles that meet these requirements are contemplated for use in the present invention. Such particles may be easily made, as described (Couvreur *et al.*,
 25 1980; 1988; zur Muhlen *et al.*, 1998; Zambaux *et al.* 1998; Pinto-Alphandry *et al.*, 1995 and U. S. Patent 5,145,684, specifically incorporated herein by reference in its entirety).

IMMUNOGENIC COMPOSITIONS

In certain preferred embodiments of the present invention, immunogenic compositions, or vaccines, are provided. The immunogenic compositions will generally comprise one or more pharmaceutical compositions, such as those discussed above, in combination with an immunostimulant. An immunostimulant may be any substance that enhances or potentiates an immune response (antibody and/or cell-mediated) to an exogenous antigen. Examples of immunostimulants include adjuvants, biodegradable microspheres (*e.g.*, polylactic galactide) and liposomes (into which the compound is incorporated; *see e.g.*, Fullerton, U.S. Patent No. 4,235,877). Vaccine preparation is generally described in, for example, M.F. Powell and M.J. Newman, eds., "Vaccine Design (the subunit and adjuvant approach)," Plenum Press (NY, 1995). Pharmaceutical compositions and immunogenic compositions within the scope of the present invention may also contain other compounds, which may be biologically active or inactive. For example, one or more immunogenic portions of other tumor antigens may be present, either incorporated into a fusion polypeptide or as a separate compound, within the composition.

Illustrative immunogenic compositions may contain DNA encoding one or more of the polypeptides as described above, such that the polypeptide is generated *in situ*. As noted above, the DNA may be present within any of a variety of delivery systems known to those of ordinary skill in the art, including nucleic acid expression systems, bacteria and viral expression systems. Numerous gene delivery techniques are well known in the art, such as those described by Rolland, *Crit. Rev. Therap. Drug Carrier Systems* 15:143-198, 1998, and references cited therein. Appropriate nucleic acid expression systems contain the necessary DNA sequences for expression in the patient (such as a suitable promoter and terminating signal). Bacterial delivery systems involve the administration of a bacterium (such as *Bacillus-Calmette-Guerrin*) that expresses an immunogenic portion of the polypeptide on its cell surface or secretes such an epitope. In a preferred embodiment, the DNA may be introduced using a viral expression system (*e.g.*, vaccinia or other pox virus, retrovirus, or adenovirus), which may involve the use of a non-pathogenic (defective), replication competent virus. Suitable systems are disclosed, for

example, in Fisher-Hoch *et al.*, *Proc. Natl. Acad. Sci. USA* 86:317-321, 1989; Flexner *et al.*, *Ann. N.Y. Acad. Sci.* 569:86-103, 1989; Flexner *et al.*, *Vaccine* 8:17-21, 1990; U.S. Patent Nos. 4,603,112, 4,769,330, and 5,017,487; WO 89/01973; U.S. Patent No. 4,777,127; GB 2,200,651; EP 0,345,242; WO 91/02805; Berkner, *Biotechniques* 5 6:616-627, 1988; Rosenfeld *et al.*, *Science* 252:431-434, 1991; Kolls *et al.*, *Proc. Natl. Acad. Sci. USA* 91:215-219, 1994; Kass-Eisler *et al.*, *Proc. Natl. Acad. Sci. USA* 90:11498-11502, 1993; Guzman *et al.*, *Circulation* 88:2838-2848, 1993; and Guzman *et al.*, *Cir. Res.* 73:1202-1207, 1993. Techniques for incorporating DNA into such expression systems are well known to those of ordinary skill in the art. The DNA may also be 10 "naked," as described, for example, in Ulmer *et al.*, *Science* 259:1745-1749, 1993 and reviewed by Cohen, *Science* 259:1691-1692, 1993. The uptake of naked DNA may be increased by coating the DNA onto biodegradable beads, which are efficiently transported into the cells. It will be apparent that an immunogenic composition may comprise both a polynucleotide and a polypeptide component. Such immunogenic compositions may 15 provide for an enhanced immune response.

It will be apparent that an immunogenic composition may contain pharmaceutically acceptable salts of the polynucleotides and polypeptides provided herein. Such salts may be prepared from pharmaceutically acceptable non-toxic bases, including organic bases (*e.g.*, salts of primary, secondary and tertiary amines and basic amino acids) 20 and inorganic bases (*e.g.*, sodium, potassium, lithium, ammonium, calcium and magnesium salts).

While any suitable carrier known to those of ordinary skill in the art may be employed in the compositions of this invention, the type of carrier will vary depending on the mode of administration. Compositions of the present invention may be formulated for 25 any appropriate manner of administration, including for example, topical, oral, nasal, intravenous, intracranial, intraperitoneal, subcutaneous or intramuscular administration. For parenteral administration, such as subcutaneous injection, the carrier preferably comprises water, saline, alcohol, a fat, a wax or a buffer. For oral administration, any of the above carriers or a solid carrier, such as mannitol, lactose, starch, magnesium stearate,

sodium saccharine, talcum, cellulose, glucose, sucrose, and magnesium carbonate, may be employed. Biodegradable microspheres (e.g., polylactate polyglycolate) may also be employed as carriers for the pharmaceutical compositions of this invention. Suitable biodegradable microspheres are disclosed, for example, in U.S. Patent Nos. 4,897,268; 5,075,109; 5,928,647; 5,811,128; 5,820,883; 5,853,763; 5,814,344 and 5,942,252. One may also employ a carrier comprising the particulate-protein complexes described in U.S. Patent No. 5,928,647, which are capable of inducing a class I-restricted cytotoxic T lymphocyte responses in a host.

Such compositions may also comprise buffers (e.g., neutral buffered saline or phosphate buffered saline), carbohydrates (e.g., glucose, mannose, sucrose or dextrans), mannitol, proteins, polypeptides or amino acids such as glycine, antioxidants, bacteriostats, chelating agents such as EDTA or glutathione, adjuvants (e.g., aluminum hydroxide), solutes that render the formulation isotonic, hypotonic or weakly hypertonic with the blood of a recipient, suspending agents, thickening agents and/or preservatives. Alternatively, compositions of the present invention may be formulated as a lyophilizate. Compounds may also be encapsulated within liposomes using well known technology.

Any of a variety of immunostimulants may be employed in the immunogenic compositions of this invention. For example, an adjuvant may be included. Most adjuvants contain a substance designed to protect the antigen from rapid catabolism, such as aluminum hydroxide or mineral oil, and a stimulator of immune responses, such as lipid A, *Bordetella pertussis* or *Mycobacterium tuberculosis* derived proteins. Suitable adjuvants are commercially available as, for example, Freund's Incomplete Adjuvant and Complete Adjuvant (Difco Laboratories, Detroit, MI); Merck Adjuvant 65 (Merck and Company, Inc., Rahway, NJ); AS-2 (SmithKline Beecham, Philadelphia, PA); aluminum salts such as aluminum hydroxide gel (alum) or aluminum phosphate; salts of calcium, iron or zinc; an insoluble suspension of acylated tyrosine; acylated sugars; cationically or anionically derivatized polysaccharides; polyphosphazenes; biodegradable microspheres; monophosphoryl lipid A and quil A. Cytokines, such as GM-CSF or interleukin-2, -7, or -12, may also be used as adjuvants.

Within the immunogenic compositions provided herein, the adjuvant composition is preferably designed to induce an immune response predominantly of the Th1 type. High levels of Th1-type cytokines (*e.g.*, IFN- γ , TNF α , IL-2 and IL-12) tend to favor the induction of cell mediated immune responses to an administered antigen. In contrast, high levels of Th2-type cytokines (*e.g.*, IL-4, IL-5, IL-6 and IL-10) tend to favor the induction of humoral immune responses. Following application of an immunogenic composition as provided herein, a patient will support an immune response that includes Th1- and Th2-type responses. Within a preferred embodiment, in which a response is predominantly Th1-type, the level of Th1-type cytokines will increase to a greater extent than the level of Th2-type cytokines. The levels of these cytokines may be readily assessed using standard assays. For a review of the families of cytokines, see Mosmann and Coffman, *Ann. Rev. Immunol.* 7:145-173, 1989.

Preferred adjuvants for use in eliciting a predominantly Th1-type response include, for example, a combination of monophosphoryl lipid A, preferably 3-de-O-acylated monophosphoryl lipid A (3D-MPL), together with an aluminum salt. MPL adjuvants are available from Corixa Corporation (Seattle, WA; *see* US Patent Nos. 4,436,727; 4,877,611; 4,866,034 and 4,912,094). CpG-containing oligonucleotides (in which the CpG dinucleotide is unmethylated) also induce a predominantly Th1 response. Such oligonucleotides are well known and are described, for example, in WO 96/02555, WO 99/33488 and U.S. Patent Nos. 6,008,200 and 5,856,462. Immunostimulatory DNA sequences are also described, for example, by Sato *et al.*, *Science* 273:352, 1996. Another preferred adjuvant is a saponin, preferably QS21 (Aquila Biopharmaceuticals Inc., Framingham, MA), which may be used alone or in combination with other adjuvants. For example, an enhanced system involves the combination of a monophosphoryl lipid A and saponin derivative, such as the combination of QS21 and 3D-MPL as described in WO 94/00153, or a less reactogenic composition where the QS21 is quenched with cholesterol, as described in WO 96/33739. Other preferred formulations comprise an oil-in-water emulsion and tocopherol. A particularly potent adjuvant formulation involving QS21, 3D-MPL and tocopherol in an oil-in-water emulsion is described in WO 95/17210.

Other preferred adjuvants include Montanide ISA 720 (Seppic, France), SAF (Chiron, California, United States), ISCOMS (CSL), MF-59 (Chiron), the SBAS series of adjuvants (*e.g.*, SBAS-2 or SBAS-4, available from SmithKline Beecham, Rixensart, Belgium), Detox (Corixa, Hamilton, MT), RC-529 (Corixa, Hamilton, MT) and
 5 other aminoalkyl glucosaminide 4-phosphates (AGPs), such as those described in pending U.S. Patent Application Serial Nos. 08/853,826 and 09/074,720, the disclosures of which are incorporated herein by reference in their entireties.

Any immunogenic composition provided herein may be prepared using well known methods that result in a combination of antigen, immune response enhancer and a
 10 suitable carrier or excipient. The compositions described herein may be administered as part of a sustained release formulation (*i.e.*, a formulation such as a capsule, sponge or gel (composed of polysaccharides, for example) that effects a slow release of compound following administration). Such formulations may generally be prepared using well known technology (*see, e.g.*, Coombes *et al.*, *Vaccine* 14:1429-1438, 1996) and administered by,
 15 for example, oral, rectal or subcutaneous implantation, or by implantation at the desired target site. Sustained-release formulations may contain a polypeptide, polynucleotide or antibody dispersed in a carrier matrix and/or contained within a reservoir surrounded by a rate controlling membrane.

Carriers for use within such formulations are biocompatible, and may also
 20 be biodegradable; preferably the formulation provides a relatively constant level of active component release. Such carriers include microparticles of poly(lactide-co-glycolide), polyacrylate, latex, starch, cellulose, dextran and the like. Other delayed-release carriers include supramolecular biovectors, which comprise a non-liquid hydrophilic core (*e.g.*, a cross-linked polysaccharide or oligosaccharide) and, optionally, an external layer
 25 comprising an amphiphilic compound, such as a phospholipid (*see e.g.*, U.S. Patent No. 5,151,254 and PCT applications WO 94/20078, WO/94/23701 and WO 96/06638). The amount of active compound contained within a sustained release formulation depends upon the site of implantation, the rate and expected duration of release and the nature of the condition to be treated or prevented.

Any of a variety of delivery vehicles may be employed within pharmaceutical compositions and immunogenic compositions to facilitate production of an antigen-specific immune response that targets tumor cells. Delivery vehicles include antigen presenting cells (APCs), such as dendritic cells, macrophages, B cells, monocytes and other cells that may be engineered to be efficient APCs. Such cells may, but need not, be genetically modified to increase the capacity for presenting the antigen, to improve activation and/or maintenance of the T cell response, to have anti-tumor effects *per se* and/or to be immunologically compatible with the receiver (*i.e.*, matched HLA haplotype). APCs may generally be isolated from any of a variety of biological fluids and organs, including tumor and peritumoral tissues, and may be autologous, allogeneic, syngeneic or xenogeneic cells.

Certain preferred embodiments of the present invention use dendritic cells or progenitors thereof as antigen-presenting cells. Dendritic cells are highly potent APCs (Banchereau and Steinman, *Nature* 392:245-251, 1998) and have been shown to be effective as a physiological adjuvant for eliciting prophylactic or therapeutic antitumor immunity (*see* Timmerman and Levy, *Ann. Rev. Med.* 50:507-529, 1999). In general, dendritic cells may be identified based on their typical shape (stellate *in situ*, with marked cytoplasmic processes (dendrites) visible *in vitro*), their ability to take up, process and present antigens with high efficiency and their ability to activate naïve T cell responses. Dendritic cells may, of course, be engineered to express specific cell-surface receptors or ligands that are not commonly found on dendritic cells *in vivo* or *ex vivo*, and such modified dendritic cells are contemplated by the present invention. As an alternative to dendritic cells, secreted vesicles antigen-loaded dendritic cells (called exosomes) may be used within an immunogenic composition (*see* Zitvogel *et al.*, *Nature Med.* 4:594-600, 1998).

Dendritic cells and progenitors may be obtained from peripheral blood, bone marrow, tumor-infiltrating cells, peritumoral tissues-infiltrating cells, lymph nodes, spleen, skin, umbilical cord blood or any other suitable tissue or fluid. For example, dendritic cells may be differentiated *ex vivo* by adding a combination of cytokines such as GM-CSF, IL-4,

IL-13 and/or TNF α to cultures of monocytes harvested from peripheral blood. Alternatively, CD34 positive cells harvested from peripheral blood, umbilical cord blood or bone marrow may be differentiated into dendritic cells by adding to the culture medium combinations of GM-CSF, IL-3, TNF α , CD40 ligand, LPS, flt3 ligand and/or other
 5 compound(s) that induce differentiation, maturation and proliferation of dendritic cells.

Dendritic cells are conveniently categorized as "immature" and "mature" cells, which allows a simple way to discriminate between two well characterized phenotypes. However, this nomenclature should not be construed to exclude all possible intermediate stages of differentiation. Immature dendritic cells are characterized as APC
 10 with a high capacity for antigen uptake and processing, which correlates with the high expression of Fc γ receptor and mannose receptor. The mature phenotype is typically characterized by a lower expression of these markers, but a high expression of cell surface molecules responsible for T cell activation such as class I and class II MHC, adhesion molecules (*e.g.*, CD54 and CD11) and costimulatory molecules (*e.g.*, CD40, CD80, CD86
 15 and 4-1BB).

APCs may generally be transfected with a polynucleotide encoding a prostate-specific protein (or portion or other variant thereof) such that the prostate-specific polypeptide, or an immunogenic portion thereof, is expressed on the cell surface. Such transfection may take place *ex vivo*, and a composition comprising such transfected cells
 20 may then be used for therapeutic purposes, as described herein. Alternatively, a gene delivery vehicle that targets a dendritic or other antigen presenting cell may be administered to a patient, resulting in transfection that occurs *in vivo*. *In vivo* and *ex vivo* transfection of dendritic cells, for example, may generally be performed using any methods known in the art, such as those described in WO 97/24447, or the gene gun approach
 25 described by Mahvi *et al.*, *Immunology and cell Biology* 75:456-460, 1997. Antigen loading of dendritic cells may be achieved by incubating dendritic cells or progenitor cells with the prostate-specific polypeptide, DNA (naked or within a plasmid vector) or RNA; or with antigen-expressing recombinant bacterium or viruses (*e.g.*, vaccinia, fowlpox, adenovirus or lentivirus vectors). Prior to loading, the polypeptide may be covalently

conjugated to an immunological partner that provides T cell help (*e.g.*, a carrier molecule). Alternatively, a dendritic cell may be pulsed with a non-conjugated immunological partner, separately or in the presence of the polypeptide.

Immunogenic compositions and pharmaceutical compositions may be presented in unit-dose or multi-dose containers, such as sealed ampoules or vials. Such containers are preferably hermetically sealed to preserve sterility of the formulation until use. In general, formulations may be stored as suspensions, solutions or emulsions in oily or aqueous vehicles. Alternatively, a immunogenic composition or pharmaceutical composition may be stored in a freeze-dried condition requiring only the addition of a sterile liquid carrier immediately prior to use.

CANCER THERAPY

In further aspects of the present invention, the compositions described herein may be used for immunotherapy of cancer, such as prostate cancer. Within such methods, pharmaceutical compositions and immunogenic compositions are typically administered to a patient. As used herein, a “patient” refers to any warm-blooded animal, preferably a human. A patient may or may not be afflicted with cancer. Accordingly, the above pharmaceutical compositions and immunogenic compositions may be used to prevent the development of a cancer or to treat a patient afflicted with a cancer. A cancer may be diagnosed using criteria generally accepted in the art, including the presence of a malignant tumor. Pharmaceutical compositions and immunogenic compositions may be administered either prior to or following surgical removal of primary tumors and/or treatment such as administration of radiotherapy or conventional chemotherapeutic drugs. Administration may be by any suitable method, including administration by intravenous, intraperitoneal, intramuscular, subcutaneous, intranasal, intradermal, anal, vaginal, topical and oral routes.

Within certain embodiments, immunotherapy may be active immunotherapy, in which treatment relies on the *in vivo* stimulation of the endogenous host

immune system to react against tumors with the administration of immune response-modifying agents (such as polypeptides and polynucleotides as provided herein).

Within other embodiments, immunotherapy may be passive immunotherapy, in which treatment involves the delivery of agents with established tumor-immune reactivity (such as effector cells or antibodies) that can directly or indirectly mediate antitumor effects and does not necessarily depend on an intact host immune system. Examples of effector cells include T cells as discussed above, T lymphocytes (such as CD8⁺ cytotoxic T lymphocytes and CD4⁺ T-helper tumor-infiltrating lymphocytes), killer cells (such as Natural Killer cells and lymphokine-activated killer cells), B cells and antigen-presenting cells (such as dendritic cells and macrophages) expressing a polypeptide provided herein. T cell receptors and antibody receptors specific for the polypeptides recited herein may be cloned, expressed and transferred into other vectors or effector cells for adoptive immunotherapy. The polypeptides provided herein may also be used to generate antibodies or anti-idiotypic antibodies (as described above and in U.S. Patent No. 4,918,164) for passive immunotherapy.

Effector cells may generally be obtained in sufficient quantities for adoptive immunotherapy by growth *in vitro*, as described herein. Culture conditions for expanding single antigen-specific effector cells to several billion in number with retention of antigen recognition *in vivo* are well known in the art. Such *in vitro* culture conditions typically use intermittent stimulation with antigen, often in the presence of cytokines (such as IL-2) and non-dividing feeder cells. As noted above, immunoreactive polypeptides as provided herein may be used to rapidly expand antigen-specific T cell cultures in order to generate a sufficient number of cells for immunotherapy. In particular, antigen-presenting cells, such as dendritic, macrophage, monocyte, fibroblast and/or B cells, may be pulsed with immunoreactive polypeptides or transfected with one or more polynucleotides using standard techniques well known in the art. For example, antigen-presenting cells can be transfected with a polynucleotide having a promoter appropriate for increasing expression in a recombinant virus or other expression system. Cultured effector cells for use in therapy must be able to grow and distribute widely, and to survive long term *in vivo*.

Studies have shown that cultured effector cells can be induced to grow *in vivo* and to survive long term in substantial numbers by repeated stimulation with antigen supplemented with IL-2 (*see, for example, Cheever et al., Immunological Reviews 157:177, 1997*).

5 Alternatively, a vector expressing a polypeptide recited herein may be introduced into antigen presenting cells taken from a patient and clonally propagated *ex vivo* for transplant back into the same patient. Transfected cells may be reintroduced into the patient using any means known in the art, preferably in sterile form by intravenous, intracavitary, intraperitoneal or intratumor administration.

10 Routes and frequency of administration of the therapeutic compositions described herein, as well as dosage, will vary from individual to individual, and may be readily established using standard techniques. In general, the pharmaceutical compositions and immunogenic compositions may be administered by injection (*e.g., intracutaneous, intramuscular, intravenous or subcutaneous*), intranasally (*e.g., by aspiration*) or orally.

15 Preferably, between 1 and 10 doses may be administered over a 52 week period. Preferably, 6 doses are administered, at intervals of 1 month, and booster vaccinations may be given periodically thereafter. Alternate protocols may be appropriate for individual patients. A suitable dose is an amount of a compound that, when administered as described above, is capable of promoting an anti-tumor immune response, and is at least 10-50%

20 above the basal (*i.e., untreated*) level. Such response can be monitored by measuring the anti-tumor antibodies in a patient or by vaccine-dependent generation of cytolytic effector cells capable of killing the patient's tumor cells *in vitro*. Such immunogenic compositions should also be capable of causing an immune response that leads to an improved clinical outcome (*e.g., more frequent remissions, complete or partial or longer disease-free*

25 survival) in treated patients as compared to non-treated patients. In general, for pharmaceutical compositions and immunogenic compositions comprising one or more polypeptides, the amount of each polypeptide present in a dose ranges from about 25 µg to 5 mg per kg of host. Suitable dose sizes will vary with the size of the patient, but will typically range from about 0.1 mL to about 5 mL.

In general, an appropriate dosage and treatment regimen provides the active compound(s) in an amount sufficient to provide therapeutic and/or prophylactic benefit. Such a response can be monitored by establishing an improved clinical outcome (*e.g.*, more frequent remissions, complete or partial, or longer disease-free survival) in treated patients as compared to non-treated patients. Increases in preexisting immune responses to a prostate-specific protein generally correlate with an improved clinical outcome. Such immune responses may generally be evaluated using standard proliferation, cytotoxicity or cytokine assays, which may be performed using samples obtained from a patient before and after treatment.

10 CANCER DETECTION AND DIAGNOSIS

In general, a cancer may be detected in a patient based on the presence of one or more prostate-specific proteins and/or polynucleotides encoding such proteins in a biological sample (for example, blood, sera, sputum urine and/or tumor biopsies) obtained from the patient. In other words, such proteins may be used as markers to indicate the presence or absence of a cancer such as prostate cancer. In addition, such proteins may be useful for the detection of other cancers. The binding agents provided herein generally permit detection of the level of antigen that binds to the agent in the biological sample. Polynucleotide primers and probes may be used to detect the level of mRNA encoding a tumor protein, which is also indicative of the presence or absence of a cancer. In general, a prostate-specific sequence should be present at a level that is at least three fold higher in prostate tissue than in other normal tissues.

There are a variety of assay formats known to those of ordinary skill in the art for using a binding agent to detect polypeptide markers in a sample. *See, e.g.*, Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In general, the presence or absence of a cancer in a patient may be determined by (a) contacting a biological sample obtained from a patient with a binding agent; (b) detecting in the sample a level of polypeptide that binds to the binding agent; and (c) comparing the level of polypeptide with a predetermined cut-off value.

In a preferred embodiment, the assay involves the use of binding agent immobilized on a solid support to bind to and remove the polypeptide from the remainder of the sample. The bound polypeptide may then be detected using a detection reagent that contains a reporter group and specifically binds to the binding agent/polypeptide complex.

5 Such detection reagents may comprise, for example, a binding agent that specifically binds to the polypeptide or an antibody or other agent that specifically binds to the binding agent, such as an anti-immunoglobulin, protein G, protein A or a lectin. Alternatively, a competitive assay may be utilized, in which a polypeptide is labeled with a reporter group and allowed to bind to the immobilized binding agent after incubation of the binding agent
10 with the sample. The extent to which components of the sample inhibit the binding of the labeled polypeptide to the binding agent is indicative of the reactivity of the sample with the immobilized binding agent. Suitable polypeptides for use within such assays include full length prostate-specific proteins and portions thereof to which the binding agent binds, as described above.

15 The solid support may be any material known to those of ordinary skill in the art to which the tumor protein may be attached. For example, the solid support may be a test well in a microtiter plate or a nitrocellulose or other suitable membrane. Alternatively, the support may be a bead or disc, such as glass, fiberglass, latex or a plastic material such as polystyrene or polyvinylchloride. The support may also be a magnetic
20 particle or a fiber optic sensor, such as those disclosed, for example, in U.S. Patent No. 5,359,681. The binding agent may be immobilized on the solid support using a variety of techniques known to those of skill in the art, which are amply described in the patent and scientific literature. In the context of the present invention, the term "immobilization" refers to both noncovalent association, such as adsorption, and covalent attachment (which
25 may be a direct linkage between the agent and functional groups on the support or may be a linkage by way of a cross-linking agent). Immobilization by adsorption to a well in a microtiter plate or to a membrane is preferred. In such cases, adsorption may be achieved by contacting the binding agent, in a suitable buffer, with the solid support for a suitable amount of time. The contact time varies with temperature, but is typically between about 1

hour and about 1 day. In general, contacting a well of a plastic microtiter plate (such as polystyrene or polyvinylchloride) with an amount of binding agent ranging from about 10 ng to about 10 μ g, and preferably about 100 ng to about 1 μ g, is sufficient to immobilize an adequate amount of binding agent.

5 Covalent attachment of binding agent to a solid support may generally be achieved by first reacting the support with a bifunctional reagent that will react with both the support and a functional group, such as a hydroxyl or amino group, on the binding agent. For example, the binding agent may be covalently attached to supports having an appropriate polymer coating using benzoquinone or by condensation of an aldehyde group
10 on the support with an amine and an active hydrogen on the binding partner (*see, e.g.*, Pierce Immunotechnology Catalog and Handbook, 1991, at A12-A13).

In certain embodiments, the assay is a two-antibody sandwich assay. This assay may be performed by first contacting an antibody that has been immobilized on a solid support, commonly the well of a microtiter plate, with the sample, such that
15 polypeptides within the sample are allowed to bind to the immobilized antibody. Unbound sample is then removed from the immobilized polypeptide-antibody complexes and a detection reagent (preferably a second antibody capable of binding to a different site on the polypeptide) containing a reporter group is added. The amount of detection reagent that remains bound to the solid support is then determined using a method appropriate for the
20 specific reporter group.

More specifically, once the antibody is immobilized on the support as described above, the remaining protein binding sites on the support are typically blocked. Any suitable blocking agent known to those of ordinary skill in the art, such as bovine serum albumin or Tween 20™ (Sigma Chemical Co., St. Louis, MO). The immobilized
25 antibody is then incubated with the sample, and polypeptide is allowed to bind to the antibody. The sample may be diluted with a suitable diluent, such as phosphate-buffered saline (PBS) prior to incubation. In general, an appropriate contact time (*i.e.*, incubation time) is a period of time that is sufficient to detect the presence of polypeptide within a sample obtained from an individual with prostate cancer. Preferably, the contact time is

sufficient to achieve a level of binding that is at least about 95% of that achieved at equilibrium between bound and unbound polypeptide. Those of ordinary skill in the art will recognize that the time necessary to achieve equilibrium may be readily determined by assaying the level of binding that occurs over a period of time. At room temperature, an incubation time of about 30 minutes is generally sufficient.

Unbound sample may then be removed by washing the solid support with an appropriate buffer, such as PBS containing 0.1% Tween 20™. The second antibody, which contains a reporter group, may then be added to the solid support. Preferred reporter groups include those groups recited above.

The detection reagent is then incubated with the immobilized antibody-polypeptide complex for an amount of time sufficient to detect the bound polypeptide. An appropriate amount of time may generally be determined by assaying the level of binding that occurs over a period of time. Unbound detection reagent is then removed and bound detection reagent is detected using the reporter group. The method employed for detecting the reporter group depends upon the nature of the reporter group. For radioactive groups, scintillation counting or autoradiographic methods are generally appropriate. Spectroscopic methods may be used to detect dyes, luminescent groups and fluorescent groups. Biotin may be detected using avidin, coupled to a different reporter group (commonly a radioactive or fluorescent group or an enzyme). Enzyme reporter groups may generally be detected by the addition of substrate (generally for a specific period of time), followed by spectroscopic or other analysis of the reaction products.

To determine the presence or absence of a cancer, such as prostate cancer, the signal detected from the reporter group that remains bound to the solid support is generally compared to a signal that corresponds to a predetermined cut-off value. In one preferred embodiment, the cut-off value for the detection of a cancer is the average mean signal obtained when the immobilized antibody is incubated with samples from patients without the cancer. In general, a sample generating a signal that is three standard deviations above the predetermined cut-off value is considered positive for the cancer. In an alternate preferred embodiment, the cut-off value is determined using a Receiver

Operator Curve, according to the method of Sackett *et al.*, *Clinical Epidemiology: A Basic Science for Clinical Medicine*, Little Brown and Co., 1985, p. 106-7. Briefly, in this embodiment, the cut-off value may be determined from a plot of pairs of true positive rates (*i.e.*, sensitivity) and false positive rates (100%-specificity) that correspond to each possible cut-off value for the diagnostic test result. The cut-off value on the plot that is the closest to the upper left-hand corner (*i.e.*, the value that encloses the largest area) is the most accurate cut-off value, and a sample generating a signal that is higher than the cut-off value determined by this method may be considered positive. Alternatively, the cut-off value may be shifted to the left along the plot, to minimize the false positive rate, or to the right, to minimize the false negative rate. In general, a sample generating a signal that is higher than the cut-off value determined by this method is considered positive for a cancer.

In a related embodiment, the assay is performed in a flow-through or strip test format, wherein the binding agent is immobilized on a membrane, such as nitrocellulose. In the flow-through test, polypeptides within the sample bind to the immobilized binding agent as the sample passes through the membrane. A second, labeled binding agent then binds to the binding agent-polypeptide complex as a solution containing the second binding agent flows through the membrane. The detection of bound second binding agent may then be performed as described above. In the strip test format, one end of the membrane to which binding agent is bound is immersed in a solution containing the sample. The sample migrates along the membrane through a region containing second binding agent and to the area of immobilized binding agent. Concentration of second binding agent at the area of immobilized antibody indicates the presence of a cancer. Typically, the concentration of second binding agent at that site generates a pattern, such as a line, that can be read visually. The absence of such a pattern indicates a negative result. In general, the amount of binding agent immobilized on the membrane is selected to generate a visually discernible pattern when the biological sample contains a level of polypeptide that would be sufficient to generate a positive signal in the two-antibody sandwich assay, in the format discussed above. Preferred binding agents for use in such assays are antibodies and antigen-binding fragments thereof. Preferably, the amount of

antibody immobilized on the membrane ranges from about 25 ng to about 1 μ g, and more preferably from about 50 ng to about 500 ng. Such tests can typically be performed with a very small amount of biological sample.

Of course, numerous other assay protocols exist that are suitable for use with the tumor proteins or binding agents of the present invention. The above descriptions are intended to be exemplary only. For example, it will be apparent to those of ordinary skill in the art that the above protocols may be readily modified to use prostate-specific polypeptides to detect antibodies that bind to such polypeptides in a biological sample. The detection of such prostate-specific protein specific antibodies may correlate with the presence of a cancer.

A cancer may also, or alternatively, be detected based on the presence of T cells that specifically react with a prostate-specific protein in a biological sample. Within certain methods, a biological sample comprising CD4⁺ and/or CD8⁺ T cells isolated from a patient is incubated with a prostate-specific polypeptide, a polynucleotide encoding such a polypeptide and/or an APC that expresses at least an immunogenic portion of such a polypeptide, and the presence or absence of specific activation of the T cells is detected. Suitable biological samples include, but are not limited to, isolated T cells. For example, T cells may be isolated from a patient by routine techniques (such as by Ficoll/Hypaque density gradient centrifugation of peripheral blood lymphocytes). T cells may be incubated *in vitro* for 2-9 days (typically 4 days) at 37°C with polypeptide (*e.g.*, 5 - 25 μ g/ml). It may be desirable to incubate another aliquot of a T cell sample in the absence of prostate-specific polypeptide to serve as a control. For CD4⁺ T cells, activation is preferably detected by evaluating proliferation of the T cells. For CD8⁺ T cells, activation is preferably detected by evaluating cytolytic activity. A level of proliferation that is at least two fold greater and/or a level of cytolytic activity that is at least 20% greater than in disease-free patients indicates the presence of a cancer in the patient.

As noted above, a cancer may also, or alternatively, be detected based on the level of mRNA encoding a prostate-specific protein in a biological sample. For example, at least two oligonucleotide primers may be employed in a polymerase chain reaction

(PCR) based assay to amplify a portion of a prostate-specific cDNA derived from a biological sample, wherein at least one of the oligonucleotide primers is specific for (*i.e.*, hybridizes to) a polynucleotide encoding the prostate-specific protein. The amplified cDNA is then separated and detected using techniques well known in the art, such as gel electrophoresis. Similarly, oligonucleotide probes that specifically hybridize to a polynucleotide encoding a prostate-specific protein may be used in a hybridization assay to detect the presence of polynucleotide encoding the tumor protein in a biological sample.

To permit hybridization under assay conditions, oligonucleotide primers and probes should comprise an oligonucleotide sequence that has at least about 60%, preferably at least about 75% and more preferably at least about 90%, identity to a portion of a polynucleotide encoding a prostate-specific protein that is at least 10 nucleotides, and preferably at least 20 nucleotides, in length. Preferably, oligonucleotide primers and/or probes hybridize to a polynucleotide encoding a polypeptide described herein under moderately stringent conditions, as defined above. Oligonucleotide primers and/or probes which may be usefully employed in the diagnostic methods described herein preferably are at least 10-40 nucleotides in length. In a preferred embodiment, the oligonucleotide primers comprise at least 10 contiguous nucleotides, more preferably at least 15 contiguous nucleotides, of a DNA molecule having a sequence recited in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823 and 824. Techniques for both PCR based assays and hybridization assays are well known in the art (*see*, for example, Mullis *et al.*, *Cold Spring Harbor Symp. Quant. Biol.*, 51:263, 1987; Erlich ed., *PCR Technology*, Stockton Press, NY, 1989).

One preferred assay employs RT-PCR, in which PCR is applied in conjunction with reverse transcription. Typically, RNA is extracted from a biological sample, such as biopsy tissue, and is reverse transcribed to produce cDNA molecules. PCR amplification using at least one specific primer generates a cDNA molecule, which may be separated and visualized using, for example, gel electrophoresis. Amplification may be performed on biological samples taken from a test patient and from an individual who is

not afflicted with a cancer. The amplification reaction may be performed on several dilutions of cDNA spanning two orders of magnitude. A two-fold or greater increase in expression in several dilutions of the test patient sample as compared to the same dilutions of the non-cancerous sample is typically considered positive.

5 In another embodiment, the compositions described herein may be used as markers for the progression of cancer. In this embodiment, assays as described above for the diagnosis of a cancer may be performed over time, and the change in the level of reactive polypeptide(s) or polynucleotide(s) evaluated. For example, the assays may be performed every 24-72 hours for a period of 6 months to 1 year, and thereafter performed
10 as needed. In general, a cancer is progressing in those patients in whom the level of polypeptide or polynucleotide detected increases over time. In contrast, the cancer is not progressing when the level of reactive polypeptide or polynucleotide either remains constant or decreases with time.

Certain *in vivo* diagnostic assays may be performed directly on a tumor.
15 One such assay involves contacting tumor cells with a binding agent. The bound binding agent may then be detected directly or indirectly via a reporter group. Such binding agents may also be used in histological applications. Alternatively, polynucleotide probes may be used within such applications.

As noted above, to improve sensitivity, multiple prostate-specific protein
20 markers may be assayed within a given sample. It will be apparent that binding agents specific for different proteins provided herein may be combined within a single assay. Further, multiple primers or probes may be used concurrently. The selection of tumor protein markers may be based on routine experiments to determine combinations that results in optimal sensitivity. In addition, or alternatively, assays for tumor proteins
25 provided herein may be combined with assays for other known tumor antigens.

DIAGNOSTIC KITS

The present invention further provides kits for use within any of the above diagnostic methods. Such kits typically comprise two or more components necessary for

performing a diagnostic assay. Components may be compounds, reagents, containers and/or equipment. For example, one container within a kit may contain a monoclonal antibody or fragment thereof that specifically binds to a prostate-specific protein. Such antibodies or fragments may be provided attached to a support material, as described

5 above. One or more additional containers may enclose elements, such as reagents or buffers, to be used in the assay. Such kits may also, or alternatively, contain a detection reagent as described above that contains a reporter group suitable for direct or indirect detection of antibody binding.

Alternatively, a kit may be designed to detect the level of mRNA encoding a

10 prostate-specific protein in a biological sample. Such kits generally comprise at least one oligonucleotide probe or primer, as described above, that hybridizes to a polynucleotide encoding a prostate-specific protein. Such an oligonucleotide may be used, for example, within a PCR or hybridization assay. Additional components that may be present within such kits include a second oligonucleotide and/or a diagnostic reagent or container to

15 facilitate the detection of a polynucleotide encoding a prostate-specific protein.

The following Examples are offered by way of illustration and not by way of limitation.

EXAMPLE 1

ISOLATION AND CHARACTERIZATION OF PROSTATE-SPECIFIC POLYPEPTIDES

This Example describes the isolation of certain prostate-specific
 5 polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library was constructed from prostate tumor poly A⁺ RNA using a Superscript Plasmid System for cDNA Synthesis and Plasmid Cloning kit (BRL Life Technologies, Gaithersburg, MD 20897) following the manufacturer's protocol. Specifically, prostate tumor tissues were homogenized with
 10 polytron (Kinematica, Switzerland) and total RNA was extracted using Trizol reagent (BRL Life Technologies) as directed by the manufacturer. The poly A⁺ RNA was then purified using a Qiagen oligotex spin column mRNA purification kit (Qiagen, Santa Clarita, CA 91355) according to the manufacturer's protocol. First-strand cDNA was synthesized using the NotI/Oligo-dT18 primer. Double-stranded cDNA was synthesized,
 15 ligated with EcoRI/BAXI adaptors (Invitrogen, San Diego, CA) and digested with NotI. Following size fractionation with Chroma Spin-1000 columns (Clontech, Palo Alto, CA), the cDNA was ligated into the EcoRI/NotI site of pCDNA3.1 (Invitrogen) and transformed into ElectroMax *E. coli* DH10B cells (BRL Life Technologies) by electroporation.

Using the same procedure, a normal human pancreas cDNA expression
 20 library was prepared from a pool of six tissue specimens (Clontech). The cDNA libraries were characterized by determining the number of independent colonies, the percentage of clones that carried insert, the average insert size and by sequence analysis. The prostate tumor library contained 1.64×10^7 independent colonies, with 70% of clones having an insert and the average insert size being 1745 base pairs. The normal pancreas cDNA
 25 library contained 3.3×10^6 independent colonies, with 69% of clones having inserts and the average insert size being 1120 base pairs. For both libraries, sequence analysis showed that the majority of clones had a full length cDNA sequence and were synthesized from mRNA, with minimal rRNA and mitochondrial DNA contamination.

cDNA library subtraction was performed using the above prostate tumor and normal pancreas cDNA libraries, as described by Hara *et al.* (*Blood*, 84:189-199, 1994) with some modifications. Specifically, a prostate tumor-specific subtracted cDNA library was generated as follows. Normal pancreas cDNA library (70 µg) was digested with
 5 EcoRI, NotI, and SfuI, followed by a filling-in reaction with DNA polymerase Klenow fragment. After phenol-chloroform extraction and ethanol precipitation, the DNA was dissolved in 100 µl of H₂O, heat-denatured and mixed with 100 µl (100 µg) of Photoprobe biotin (Vector Laboratories, Burlingame, CA). As recommended by the manufacturer, the resulting mixture was irradiated with a 270 W sunlamp on ice for 20 minutes. Additional
 10 Photoprobe biotin (50 µl) was added and the biotinylation reaction was repeated. After extraction with butanol five times, the DNA was ethanol-precipitated and dissolved in 23 µl H₂O to form the driver DNA.

To form the tracer DNA, 10 µg prostate tumor cDNA library was digested with BamHI and XhoI, phenol chloroform extracted and passed through Chroma spin-400
 15 columns (Clontech). Following ethanol precipitation, the tracer DNA was dissolved in 5 µl H₂O. Tracer DNA was mixed with 15 µl driver DNA and 20 µl of 2 x hybridization buffer (1.5 M NaCl/10 mM EDTA/50 mM HEPES pH 7.5/0.2% sodium dodecyl sulfate), overlaid with mineral oil, and heat-denatured completely. The sample was immediately transferred into a 68 °C water bath and incubated for 20 hours (long hybridization [LH]). The reaction
 20 mixture was then subjected to a streptavidin treatment followed by phenol/chloroform extraction. This process was repeated three more times. Subtracted DNA was precipitated, dissolved in 12 µl H₂O, mixed with 8 µl driver DNA and 20 µl of 2 x hybridization buffer, and subjected to a hybridization at 68 °C for 2 hours (short hybridization [SH]). After removal of biotinylated double-stranded DNA, subtracted cDNA was ligated into
 25 BamHI/XhoI site of chloramphenicol resistant pBCSK⁺ (Stratagene, La Jolla, CA 92037) and transformed into ElectroMax *E. coli* DH10B cells by electroporation to generate a prostate tumor specific subtracted cDNA library (referred to as “prostate subtraction 1”).

To analyze the subtracted cDNA library, plasmid DNA was prepared from 100 independent clones, randomly picked from the subtracted prostate tumor specific

library and grouped based on insert size. Representative cDNA clones were further characterized by DNA sequencing with a Perkin Elmer/Applied Biosystems Division Automated Sequencer Model 373A (Foster City, CA). Six cDNA clones, hereinafter referred to as F1-13, F1-12, F1-16, H1-1, H1-9 and H1-4, were shown to be abundant in the subtracted prostate-specific cDNA library. The determined 3' and 5' cDNA sequences for F1-12 are provided in SEQ ID NO: 2 and 3, respectively, with determined 3' cDNA sequences for F1-13, F1-16, H1-1, H1-9 and H1-4 being provided in SEQ ID NO: 1 and 4-7, respectively.

The cDNA sequences for the isolated clones were compared to known sequences in the gene bank using the EMBL and GenBank databases (release 96). Four of the prostate tumor cDNA clones, F1-13, F1-16, H1-1, and H1-4, were determined to encode the following previously identified proteins: prostate specific antigen (PSA), human glandular kallikrein, human tumor expression enhanced gene, and mitochondria cytochrome C oxidase subunit II. H1-9 was found to be identical to a previously identified human autonomously replicating sequence. No significant homologies to the cDNA sequence for F1-12 were found.

Subsequent studies led to the isolation of a full-length cDNA sequence for F1-12 (also referred to as P504S). This sequence is provided in SEQ ID NO: 107, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 108. cDNA splice variants of P504S are provided in SEQ ID NO: 600-605.

To clone less abundant prostate tumor specific genes, cDNA library subtraction was performed by subtracting the prostate tumor cDNA library described above with the normal pancreas cDNA library and with the three most abundant genes in the previously subtracted prostate tumor specific cDNA library: human glandular kallikrein, prostate specific antigen (PSA), and mitochondria cytochrome C oxidase subunit II. Specifically, 1 µg each of human glandular kallikrein, PSA and mitochondria cytochrome C oxidase subunit II cDNAs in pCDNA3.1 were added to the driver DNA and subtraction was performed as described above to provide a second subtracted cDNA library hereinafter referred to as the "subtracted prostate tumor specific cDNA library with spike".

Twenty-two cDNA clones were isolated from the subtracted prostate tumor specific cDNA library with spike. The determined 3' and 5' cDNA sequences for the clones referred to as J1-17, L1-12, N1-1862, J1-13, J1-19, J1-25, J1-24, K1-58, K1-63, L1-4 and L1-14 are provided in SEQ ID NOS: 8-9, 10-11, 12-13, 14-15, 16-17, 18-19, 20-21, 22-23, 24-25, 26-27 and 28-29, respectively. The determined 3' cDNA sequences for the clones referred to as J1-12, J1-16, J1-21, K1-48, K1-55, L1-2, L1-6, N1-1858, N1-1860, N1-1861, N1-1864 are provided in SEQ ID NOS: 30-40, respectively. Comparison of these sequences with those in the gene bank as described above, revealed no significant homologies to three of the five most abundant DNA species, (J1-17, L1-12 and N1-1862; SEQ ID NOS: 8-9, 10-11 and 12-13, respectively). Of the remaining two most abundant species, one (J1-12; SEQ ID NO:30) was found to be identical to the previously identified human pulmonary surfactant-associated protein, and the other (K1-48; SEQ ID NO:33) was determined to have some homology to *R. norvegicus* mRNA for 2-arylpropionyl-CoA epimerase. Of the 17 less abundant cDNA clones isolated from the subtracted prostate tumor specific cDNA library with spike, four (J1-16, K1-55, L1-6 and N1-1864; SEQ ID NOS:31, 34, 36 and 40, respectively) were found to be identical to previously identified sequences, two (J1-21 and N1-1860; SEQ ID NOS: 32 and 38, respectively) were found to show some homology to non-human sequences, and two (L1-2 and N1-1861; SEQ ID NOS: 35 and 39, respectively) were found to show some homology to known human sequences. No significant homologies were found to the polypeptides J1-13, J1-19, J1-24, J1-25, K1-58, K1-63, L1-4, L1-14 (SEQ ID NOS: 14-15, 16-17, 20-21, 18-19, 22-23, 24-25, 26-27, 28-29, respectively).

Subsequent studies led to the isolation of full length cDNA sequences for J1-17, L1-12 and N1-1862 (SEQ ID NOS: 109-111, respectively). The corresponding predicted amino acid sequences are provided in SEQ ID NOS: 112-114. L1-12 is also referred to as P501S. A cDNA splice variant of P501S is provided in SEQ ID NO: 606.

In a further experiment, four additional clones were identified by subtracting a prostate tumor cDNA library with normal prostate cDNA prepared from a pool of three normal prostate poly A+ RNA (referred to as "prostate subtraction 2"). The determined

cDNA sequences for these clones, hereinafter referred to as U1-3064, U1-3065, V1-3692 and 1A-3905, are provided in SEQ ID NO: 69-72, respectively. Comparison of the determined sequences with those in the gene bank revealed no significant homologies to U1-3065.

5 A second subtraction with spike (referred to as “prostate subtraction spike 2”) was performed by subtracting a prostate tumor specific cDNA library with spike with normal pancreas cDNA library and further spiked with PSA, J1-17, pulmonary surfactant-associated protein, mitochondrial DNA, cytochrome c oxidase subunit II, N1-1862, autonomously replicating sequence, L1-12 and tumor expression enhanced gene. Four
10 additional clones, hereinafter referred to as V1-3686, R1-2330, 1B-3976 and V1-3679, were isolated. The determined cDNA sequences for these clones are provided in SEQ ID NO:73-76, respectively. Comparison of these sequences with those in the gene bank revealed no significant homologies to V1-3686 and R1-2330.

 Further analysis of the three prostate subtractions described above (prostate
15 subtraction 2, subtracted prostate tumor specific cDNA library with spike, and prostate subtraction spike 2) resulted in the identification of sixteen additional clones, referred to as 1G-4736, 1G-4738, 1G-4741, 1G-4744, 1G-4734, 1H-4774, 1H-4781, 1H-4785, 1H-4787, 1H-4796, 1I-4810, 1I-4811, 1J-4876, 1K-4884 and 1K-4896. The determined cDNA sequences for these clones are provided in SEQ ID NOS: 77-92, respectively. Comparison
20 of these sequences with those in the gene bank as described above, revealed no significant homologies to 1G-4741, 1G-4734, 1I-4807, 1J-4876 and 1K-4896 (SEQ ID NOS: 79, 81, 87, 90 and 92, respectively). Further analysis of the isolated clones led to the determination of extended cDNA sequences for 1G-4736, 1G-4738, 1G-4741, 1G-4744, 1H-4774, 1H-4781, 1H-4785, 1H-4787, 1H-4796, 1I-4807, 1J-4876, 1K-4884 and 1K-
25 4896, provided in SEQ ID NOS: 179-188 and 191-193, respectively, and to the determination of additional partial cDNA sequences for 1I-4810 and 1I-4811, provided in SEQ ID NOS: 189 and 190, respectively.

 Additional studies with prostate subtraction spike 2 resulted in the isolation of three more clones. Their sequences were determined as described above and compared

to the most recent GenBank. All three clones were found to have homology to known genes, which are Cysteine-rich protein, KIAA0242, and KIAA0280 (SEQ ID NO: 317, 319, and 320, respectively). Further analysis of these clones by Synteni microarray (Synteni, Palo Alto, CA) demonstrated that all three clones were over-expressed in most prostate tumors and prostate BPH, as well as in the majority of normal prostate tissues tested, but low expression in all other normal tissues.

An additional subtraction was performed by subtracting a normal prostate cDNA library with normal pancreas cDNA (referred to as "prostate subtraction 3"). This led to the identification of six additional clones referred to as 1G-4761, 1G-4762, 1H-4766, 1H-4770, 1H-4771 and 1H-4772 (SEQ ID NOS: 93-98). Comparison of these sequences with those in the gene bank revealed no significant homologies to 1G-4761 and 1H-4771 (SEQ ID NOS: 93 and 97, respectively). Further analysis of the isolated clones led to the determination of extended cDNA sequences for 1G-4761, 1G-4762, 1H-4766 and 1H-4772 provided in SEQ ID NOS: 194-196 and 199, respectively, and to the determination of additional partial cDNA sequences for 1H-4770 and 1H-4771, provided in SEQ ID NOS: 197 and 198, respectively.

Subtraction of a prostate tumor cDNA library, prepared from a pool of polyA⁺ RNA from three prostate cancer patients, with a normal pancreas cDNA library (prostate subtraction 4) led to the identification of eight clones, referred to as 1D-4297, 1D-4309, 1D-4278, 1D-4288, 1D-4283, 1D-4304, 1D-4296 and 1D-4280 (SEQ ID NOS: 99-107). These sequences were compared to those in the gene bank as described above. No significant homologies were found to 1D-4283 and 1D-4304 (SEQ ID NOS: 103 and 104, respectively). Further analysis of the isolated clones led to the determination of extended cDNA sequences for 1D-4309, 1D-4278, 1D-4288, 1D-4283, 1D-4304, 1D-4296 and 1D-4280, provided in SEQ ID NOS: 200-206, respectively.

cDNA clones isolated in prostate subtraction 1 and prostate subtraction 2, described above, were colony PCR amplified and their mRNA expression levels in prostate tumor, normal prostate and in various other normal tissues were determined using microarray technology (Synteni, Palo Alto, CA). Briefly, the PCR amplification products

were dotted onto slides in an array format, with each product occupying a unique location in the array. mRNA was extracted from the tissue sample to be tested, reverse transcribed, and fluorescent-labeled cDNA probes were generated. The microarrays were probed with the labeled cDNA probes, the slides scanned and fluorescence intensity was measured.

- 5 This intensity correlates with the hybridization intensity. Two clones (referred to as P509S and P510S) were found to be over-expressed in prostate tumor and normal prostate and expressed at low levels in all other normal tissues tested (liver, pancreas, skin, bone marrow, brain, breast, adrenal gland, bladder, testes, salivary gland, large intestine, kidney, ovary, lung, spinal cord, skeletal muscle and colon). The determined cDNA sequences for
- 10 P509S and P510S are provided in SEQ ID NO: 223 and 224, respectively. Comparison of these sequences with those in the gene bank as described above, revealed some homology to previously identified ESTs.

- Additional, studies led to the isolation of the full-length cDNA sequence for P509S. This sequence is provided in SEQ ID NO: 332, with the corresponding predicted
- 15 amino acid sequence being provided in SEQ ID NO: 339. Two variant full-length cDNA sequences for P510S are provided in SEQ ID NO: 535 and 536, with the corresponding predicted amino acid sequences being provided in SEQ ID NO: 537 and 538, respectively. Additional splice variants of P510S are provided in SEQ ID NO: 598 and 599.

- The determined cDNA sequences for additional prostate-specific clones
- 20 isolated during characterization of prostate specific cDNA libraries are provided in SEQ ID NO: 618-689, 691-697 and 709-772. Comparison of these sequences with those in the public databases revealed no significant homologies to any of these sequences.

EXAMPLE 2

25 DETERMINATION OF TISSUE SPECIFICITY OF PROSTATE-SPECIFIC POLYPEPTIDES

Using gene specific primers, mRNA expression levels for the representative prostate-specific polypeptides F1-16, H1-1, J1-17 (also referred to as P502S), L1-12 (also

referred to as P501S), F1-12 (also referred to as P504S) and N1-1862 (also referred to as P503S) were examined in a variety of normal and tumor tissues using RT-PCR.

Briefly, total RNA was extracted from a variety of normal and tumor tissues using Trizol reagent as described above. First strand synthesis was carried out using 1-2
 5 μ g of total RNA with SuperScript II reverse transcriptase (BRL Life Technologies) at 42^oC for one hour. The cDNA was then amplified by PCR with gene-specific primers. To ensure the semi-quantitative nature of the RT-PCR, β -actin was used as an internal control for each of the tissues examined. First, serial dilutions of the first strand cDNAs were prepared and RT-PCR assays were performed using β -actin specific primers. A dilution
 10 was then chosen that enabled the linear range amplification of the β -actin template and which was sensitive enough to reflect the differences in the initial copy numbers. Using these conditions, the β -actin levels were determined for each reverse transcription reaction from each tissue. DNA contamination was minimized by DNase treatment and by assuring a negative PCR result when using first strand cDNA that was prepared without adding
 15 reverse transcriptase.

mRNA Expression levels were examined in four different types of tumor tissue (prostate tumor from 2 patients, breast tumor from 3 patients, colon tumor, lung tumor), and sixteen different normal tissues, including prostate, colon, kidney, liver, lung, ovary, pancreas, skeletal muscle, skin, stomach, testes, bone marrow and brain. F1-16 was
 20 found to be expressed at high levels in prostate tumor tissue, colon tumor and normal prostate, and at lower levels in normal liver, skin and testes, with expression being undetectable in the other tissues examined. H1-1 was found to be expressed at high levels in prostate tumor, lung tumor, breast tumor, normal prostate, normal colon and normal brain, at much lower levels in normal lung, pancreas, skeletal muscle, skin, small intestine,
 25 bone marrow, and was not detected in the other tissues tested. J1-17 (P502S) and L1-12 (P501S) appear to be specifically over-expressed in prostate, with both genes being expressed at high levels in prostate tumor and normal prostate but at low to undetectable levels in all the other tissues examined. N1-1862 (P503S) was found to be over-expressed in 60% of prostate tumors and detectable in normal colon and kidney. The RT-PCR results

thus indicate that F1-16, H1-1, J1-17 (P502S), N1-1862 (P503S) and L1-12 (P501S) are either prostate specific or are expressed at significantly elevated levels in prostate.

Further RT-PCR studies showed that F1-12 (P504S) is over-expressed in 60% of prostate tumors, detectable in normal kidney but not detectable in all other tissues tested. Similarly, R1-2330 was shown to be over-expressed in 40% of prostate tumors, detectable in normal kidney and liver, but not detectable in all other tissues tested. U1-3064 was found to be over-expressed in 60% of prostate tumors, and also expressed in breast and colon tumors, but was not detectable in normal tissues.

RT-PCR characterization of R1-2330, U1-3064 and 1D-4279 showed that these three antigens are over-expressed in prostate and/or prostate tumors.

Northern analysis with four prostate tumors, two normal prostate samples, two BPH prostates, and normal colon, kidney, liver, lung, pancreas, skeletal muscle, brain, stomach, testes, small intestine and bone marrow, showed that L1-12 (P501S) is over-expressed in prostate tumors and normal prostate, while being undetectable in other normal tissues tested. J1-17 (P502S) was detected in two prostate tumors and not in the other tissues tested. N1-1862 (P503S) was found to be over-expressed in three prostate tumors and to be expressed in normal prostate, colon and kidney, but not in other tissues tested. F1-12 (P504S) was found to be highly expressed in two prostate tumors and to be undetectable in all other tissues tested.

The microarray technology described above was used to determine the expression levels of representative antigens described herein in prostate tumor, breast tumor and the following normal tissues: prostate, liver, pancreas, skin, bone marrow, brain, breast, adrenal gland, bladder, testes, salivary gland, large intestine, kidney, ovary, lung, spinal cord, skeletal muscle and colon. L1-12 (P501S) was found to be over-expressed in normal prostate and prostate tumor, with some expression being detected in normal skeletal muscle. Both J1-12 and F1-12 (P504S) were found to be over-expressed in prostate tumor, with expression being lower or undetectable in all other tissues tested. N1-1862 (P503S) was found to be expressed at high levels in prostate tumor and normal prostate, and at low levels in normal large intestine and normal colon, with expression

being undetectable in all other tissues tested. R1-2330 was found to be over-expressed in prostate tumor and normal prostate, and to be expressed at lower levels in all other tissues tested. 1D-4279 was found to be over-expressed in prostate tumor and normal prostate, expressed at lower levels in normal spinal cord, and to be undetectable in all other tissues
5 tested.

Further microarray analysis to specifically address the extent to which P501S (SEQ ID NO: 110) was expressed in breast tumor revealed moderate over-expression not only in breast tumor, but also in metastatic breast tumor (2/31), with negligible to low expression in normal tissues. This data suggests that P501S may be over-
10 expressed in various breast tumors as well as in prostate tumors.

The expression levels of 32 ESTs (expressed sequence tags) described by Vasmatazis *et al.* (*Proc. Natl. Acad. Sci. USA* 95:300-304, 1998) in a variety of tumor and normal tissues were examined by microarray technology as described above. Two of these clones (referred to as P1000C and P1001C) were found to be over-expressed in prostate
15 tumor and normal prostate, and expressed at low to undetectable levels in all other tissues tested (normal aorta, thymus, resting and activated PBMC, epithelial cells, spinal cord, adrenal gland, fetal tissues, skin, salivary gland, large intestine, bone marrow, liver, lung, dendritic cells, stomach, lymph nodes, brain, heart, small intestine, skeletal muscle, colon and kidney. The determined cDNA sequences for P1000C and P1001C are provided in
20 SEQ ID NO: 384 and 472, respectively. The sequence of P1001C was found to show some homology to the previously isolated Human mRNA for JM27 protein. No significant homologies were found to the sequence of P1000C.

The expression of the polypeptide encoded by the full length cDNA sequence for F1-12 (also referred to as P504S; SEQ ID NO: 108) was investigated by
25 immunohistochemical analysis. Rabbit-anti-P504S polyclonal antibodies were generated against the full length P504S protein by standard techniques. Subsequent isolation and characterization of the polyclonal antibodies were also performed by techniques well known in the art. Immunohistochemical analysis showed that the P504S polypeptide was expressed in 100% of prostate carcinoma samples tested (n=5).

The rabbit-anti-P504S polyclonal antibody did not appear to label benign prostate cells with the same cytoplasmic granular staining, but rather with light nuclear staining. Analysis of normal tissues revealed that the encoded polypeptide was found to be expressed in some, but not all normal human tissues. Positive cytoplasmic staining with
 5 rabbit-anti-P504S polyclonal antibody was found in normal human kidney, liver, brain, colon and lung-associated macrophages, whereas heart and bone marrow were negative.

This data indicates that the P504S polypeptide is present in prostate cancer tissues, and that there are qualitative and quantitative differences in the staining between benign prostatic hyperplasia tissues and prostate cancer tissues, suggesting that this
 10 polypeptide may be detected selectively in prostate tumors and therefore be useful in the diagnosis of prostate cancer.

EXAMPLE 3

ISOLATION AND CHARACTERIZATION OF PROSTATE-SPECIFIC 15 POLYPEPTIDES BY PCR-BASED SUBTRACTION

A cDNA subtraction library, containing cDNA from normal prostate subtracted with ten other normal tissue cDNAs (brain, heart, kidney, liver, lung, ovary, placenta, skeletal muscle, spleen and thymus) and then submitted to a first round of PCR
 20 amplification, was purchased from Clontech. This library was subjected to a second round of PCR amplification, following the manufacturer's protocol. The resulting cDNA fragments were subcloned into the vector pT7 Blue T-vector (Novagen, Madison, WI) and transformed into XL-1 Blue MRF' *E. coli* (Stratagene). DNA was isolated from independent clones and sequenced using a Perkin Elmer/Applied Biosystems Division
 25 Automated Sequencer Model 373A.

Fifty-nine positive clones were sequenced. Comparison of the DNA sequences of these clones with those in the gene bank, as described above, revealed no significant homologies to 25 of these clones, hereinafter referred to as P5, P8, P9, P18, P20, P30, P34, P36, P38, P39, P42, P49, P50, P53, P55, P60, P64, P65, P73, P75, P76, P79

and P84. The determined cDNA sequences for these clones are provided in SEQ ID NO: 41-45, 47-52 and 54-65, respectively. P29, P47, P68, P80 and P82 (SEQ ID NO: 46, 53 and 66-68, respectively) were found to show some degree of homology to previously identified DNA sequences. To the best of the inventors' knowledge, none of these
5 sequences have been previously shown to be present in prostate.

Further studies employing the sequence of SEQ ID NO: 67 as a probe in standard full-length cloning methods, resulted in the isolation of three cDNA sequences which appear to be splice variants of P80 (also known as P704P). These sequences are provided in SEQ ID NO: 699-701.

10 Further studies using the PCR-based methodology described above resulted in the isolation of more than 180 additional clones, of which 23 clones were found to show no significant homologies to known sequences. The determined cDNA sequences for these clones are provided in SEQ ID NO: 115-123, 127, 131, 137, 145, 147-151, 153, 156-158 and 160. Twenty-three clones (SEQ ID NO: 124-126, 128-130, 132-136, 138-144, 146,
15 152, 154, 155 and 159) were found to show some homology to previously identified ESTs. An additional ten clones (SEQ ID NO: 161-170) were found to have some degree of homology to known genes. Larger cDNA clones containing the P20 sequence represent splice variants of a gene referred to as P703P. The determined DNA sequence for the variants referred to as DE1, DE13 and DE14 are provided in SEQ ID NOS: 171, 175 and
20 177, respectively, with the corresponding predicted amino acid sequences being provided in SEQ ID NO: 172, 176 and 178, respectively. The determined cDNA sequence for an extended spliced form of P703 is provided in SEQ ID NO: 225. The DNA sequences for the splice variants referred to as DE2 and DE6 are provided in SEQ ID NOS: 173 and 174, respectively.

25 mRNA Expression levels for representative clones in tumor tissues (prostate (n=5), breast (n=2), colon and lung) normal tissues (prostate (n=5), colon, kidney, liver, lung (n=2), ovary (n=2), skeletal muscle, skin, stomach, small intestine and brain), and activated and non-activated PBMC was determined by RT-PCR as described above. Expression was examined in one sample of each tissue type unless otherwise indicated.

P9 was found to be highly expressed in normal prostate and prostate tumor compared to all normal tissues tested except for normal colon which showed comparable expression. P20, a portion of the P703P gene, was found to be highly expressed in normal prostate and prostate tumor, compared to all twelve normal tissues tested. A modest increase in expression of P20 in breast tumor (n=2), colon tumor and lung tumor was seen compared to all normal tissues except lung (1 of 2). Increased expression of P18 was found in normal prostate, prostate tumor and breast tumor compared to other normal tissues except lung and stomach. A modest increase in expression of P5 was observed in normal prostate compared to most other normal tissues. However, some elevated expression was seen in normal lung and PBMC. Elevated expression of P5 was also observed in prostate tumors (2 of 5), breast tumor and one lung tumor sample. For P30, similar expression levels were seen in normal prostate and prostate tumor, compared to six of twelve other normal tissues tested. Increased expression was seen in breast tumors, one lung tumor sample and one colon tumor sample, and also in normal PBMC. P29 was found to be over-expressed in prostate tumor (5 of 5) and normal prostate (5 of 5) compared to the majority of normal tissues. However, substantial expression of P29 was observed in normal colon and normal lung (2 of 2). P80 was found to be over-expressed in prostate tumor (5 of 5) and normal prostate (5 of 5) compared to all other normal tissues tested, with increased expression also being seen in colon tumor.

Further studies resulted in the isolation of twelve additional clones, hereinafter referred to as 10-d8, 10-h10, 11-c8, 7-g6, 8-b5, 8-b6, 8-d4, 8-d9, 8-g3, 8-h11, 9-f12 and 9-f3. The determined DNA sequences for 10-d8, 10-h10, 11-c8, 8-d4, 8-d9, 8-h11, 9-f12 and 9-f3 are provided in SEQ ID NO: 207, 208, 209, 216, 217, 220, 221 and 222, respectively. The determined forward and reverse DNA sequences for 7-g6, 8-b5, 8-b6 and 8-g3 are provided in SEQ ID NO: 210 and 211; 212 and 213; 214 and 215; and 218 and 219, respectively. Comparison of these sequences with those in the gene bank revealed no significant homologies to the sequence of 9-f3. The clones 10-d8, 11-c8 and 8-h11 were found to show some homology to previously isolated ESTs, while 10-h10, 8-b5, 8-b6, 8-d4, 8-d9, 8-g3 and 9-f12 were found to show some homology to previously identified genes.

Further characterization of 7-G6 and 8-G3 showed identity to the known genes PAP and PSA, respectively.

mRNA expression levels for these clones were determined using the micro-array technology described above. The clones 7-G6, 8-G3, 8-B5, 8-B6, 8-D4, 8-D9, 9-F3, 9-F12, 9-H3, 10-A2, 10-A4, 11-C9 and 11-F2 were found to be over-expressed in prostate tumor and normal prostate, with expression in other tissues tested being low or undetectable. Increased expression of 8-F11 was seen in prostate tumor and normal prostate, bladder, skeletal muscle and colon. Increased expression of 10-H10 was seen in prostate tumor and normal prostate, bladder, lung, colon, brain and large intestine. Increased expression of 9-B1 was seen in prostate tumor, breast tumor, and normal prostate, salivary gland, large intestine and skin, with increased expression of 11-C8 being seen in prostate tumor, and normal prostate and large intestine.

An additional cDNA fragment derived from the PCR-based normal prostate subtraction, described above, was found to be prostate specific by both micro-array technology and RT-PCR. The determined cDNA sequence of this clone (referred to as 9-A11) is provided in SEQ ID NO: 226. Comparison of this sequence with those in the public databases revealed 99% identity to the known gene HOXB13.

Further studies led to the isolation of the clones 8-C6 and 8-H7. The determined cDNA sequences for these clones are provided in SEQ ID NO: 227 and 228, respectively. These sequences were found to show some homology to previously isolated ESTs.

PCR and hybridization-based methodologies were employed to obtain longer cDNA sequences for clone P20 (also referred to as P703P), yielding three additional cDNA fragments that progressively extend the 5' end of the gene. These fragments, referred to as P703PDE5, P703P6.26, and P703PX-23 (SEQ ID NO: 326, 328 and 330, with the predicted corresponding amino acid sequences being provided in SEQ ID NO: 327, 329 and 331, respectively) contain additional 5' sequence. P703PDE5 was recovered by screening of a cDNA library (#141-26) with a portion of P703P as a probe. P703P6.26 was recovered from a mixture of three prostate tumor cDNAs and P703PX_23 was

recovered from cDNA library (#438-48). Together, the additional sequences include all of the putative mature serine protease along with part of the putative signal sequence. The full-length cDNA sequence for P703P is provided in SEQ ID NO: 524, with the corresponding amino acid sequence being provided in SEQ ID NO: 525.

5 P703P was found to show some homology to previously identified proteases, such as thrombin. The thrombin receptor has been shown to be preferentially expressed in highly metastatic breast carcinoma cells and breast carcinoma biopsy samples. Introduction of thrombin receptor antisense cDNA has been shown to inhibit the invasion of metastatic breast carcinoma cells in culture. Antibodies against thrombin receptor
10 inhibit thrombin receptor activation and thrombin-induced platelet activation. Furthermore, peptides that resemble the receptor's tethered ligand domain inhibit platelet aggregation by thrombin. P703P may play a role in prostate cancer through a protease-activated receptor on the cancer cell or on stromal cells. The potential trypsin-like protease activity of P703P may either activate a protease-activated receptor on the cancer cell
15 membrane to promote tumorigenesis or activate a protease-activated receptor on the adjacent cells (such as stromal cells) to secrete growth factors and/or proteases (such as matrix metalloproteinases) that could promote tumor angiogenesis, invasion and metastasis. P703P may thus promote tumor progression and/or metastasis through the activation of protease-activated receptor. Polypeptides and antibodies that block the
20 P703P-receptor interaction may therefore be usefully employed in the treatment of prostate cancer.

To determine whether P703P expression increases with increased severity of Gleason grade, an indicator of tumor stage, quantitative PCR analysis was performed on prostate tumor samples with a range of Gleason scores from 5 to > 8. The mean level of
25 P703P expression increased with increasing Gleason score, indicating that P703P expression may correlate with increased disease severity.

Further studies using a PCR-based subtraction library of a prostate tumor pool subtracted against a pool of normal tissues (referred to as JP: PCR subtraction) resulted in the isolation of thirteen additional clones, seven of which did not share any

significant homology to known GenBank sequences. The determined cDNA sequences for these seven clones (P711P, P712P, novel 23, P774P, P775P, P710P and P768P) are provided in SEQ ID NO: 307-311, 313 and 315, respectively. The remaining six clones (SEQ ID NO: 316 and 321-325) were shown to share some homology to known genes. By
5 microarray analysis, all thirteen clones showed three or more fold over-expression in prostate tissues, including prostate tumors, BPH and normal prostate as compared to normal non-prostate tissues. Clones P711P, P712P, novel 23 and P768P showed over-expression in most prostate tumors and BPH tissues tested (n=29), and in the majority of normal prostate tissues (n=4), but background to low expression levels in all normal
10 tissues. Clones P774P, P775P and P710P showed comparatively lower expression and expression in fewer prostate tumors and BPH samples, with negative to low expression in normal prostate.

Further studies led to the isolation of an extended cDNA sequence for P712P (SEQ ID NO: 552). The amino acid sequences encoded by 16 predicted open
15 reading frames present within the sequence of SEQ ID NO: 552 are provided in SEQ ID NO: 553-568.

The full-length cDNA for P711P was obtained by employing the partial sequence of SEQ ID NO: 307 to screen a prostate cDNA library. Specifically, a directionally cloned prostate cDNA library was prepared using standard techniques. One
20 million colonies of this library were plated onto LB/Amp plates. Nylon membrane filters were used to lift these colonies, and the cDNAs which were picked up by these filters were denatured and cross-linked to the filters by UV light. The P711P cDNA fragment of SEQ ID NO: 307 was radio-labeled and used to hybridize with these filters. Positive clones were selected, and cDNAs were prepared and sequenced using an automatic Perkin
25 Elmer/Applied Biosystems sequencer. The determined full-length sequence of P711P is provided in SEQ ID NO: 382, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 383.

Using PCR and hybridization-based methodologies, additional cDNA sequence information was derived for two clones described above, 11-C9 and 9-F3, herein

after referred to as P707P and P714P, respectively (SEQ ID NO: 333 and 334). After comparison with the most recent GenBank, P707P was found to be a splice variant of the known gene HoxB13. In contrast, no significant homologies to P714P were found. Further studies employing the sequence of SEQ ID NO: 334 as a probe in standard full-length cloning methods, resulted in an extended cDNA sequence for P714P. This sequence is provided in SEQ ID NO: 698. This sequence was found to show some homology to the gene that encodes human ribosomal L23A protein.

Clones 8-B3, P89, P98, P130 and P201 (as disclosed in U.S. Patent Application No. 09/020,956, filed February 9, 1998) were found to be contained within one contiguous sequence, referred to as P705P (SEQ ID NO: 335, with the predicted amino acid sequence provided in SEQ ID NO: 336), which was determined to be a splice variant of the known gene NKX 3.1.

Further studies on P775P resulted in the isolation of four additional sequences (SEQ ID NO: 473-476) which are all splice variants of the P775P gene. The sequence of SEQ ID NO: 474 was found to contain two open reading frames (ORFs). The predicted amino acid sequences encoded by these ORFs are provided in SEQ ID NO: 477 and 478. The cDNA sequence of SEQ ID NO: 475 was found to contain an ORF which encodes the amino acid sequence of SEQ ID NO: 479. The cDNA sequence of SEQ ID NO: 473 was found to contain four ORFs. The predicted amino acid sequences encoded by these ORFs are provided in SEQ ID NO: 480-483. Additional splice variants of P775P are provided in SEQ ID NO: 593-597.

Subsequent studies led to the identification of a genomic region on chromosome 22q11.2, known as the Cat Eye Syndrome region, that contains the five prostate genes P704P, P712P, P774P, P775P and B305D. The relative location of each of these five genes within the genomic region is shown in Fig. 10. This region may therefore be associated with malignant tumors, and other potential tumor genes may be contained within this region. These studies also led to the identification of a potential open reading frame (ORF) for P775P (provided in SEQ ID NO: 533), which encodes the amino acid sequence of SEQ ID NO: 534.

Comparison of the clone of SEQ ID NO: 325 (referred to as P558S) with sequences in the GenBank and GeneSeq DNA databases showed that P558S is identical to the prostate-specific transglutaminase gene, which is known to have two forms. The full-length sequences for the two forms are provided in SEQ ID NO: 773 and 774, with the corresponding amino acid sequences being provided in SEQ ID NO: 775 and 776, respectively. The cDNA sequence of SEQ ID NO: 774 has a 15 pair base insert, resulting in a 5 amino acid insert in the corresponding amino acid sequence (SEQ ID NO: 776). This insert is not present in the sequence of SEQ ID NO: 773.

EXAMPLE 4

SYNTHESIS OF POLYPEPTIDES

Polypeptides may be synthesized on a Perkin Elmer/Applied Biosystems 430A peptide synthesizer using FMOC chemistry with HPTU (O-Benzotriazole-N,N,N',N'-tetramethyluronium hexafluorophosphate) activation. A Gly-Cys-Gly sequence may be attached to the amino terminus of the peptide to provide a method of conjugation, binding to an immobilized surface, or labeling of the peptide. Cleavage of the peptides from the solid support may be carried out using the following cleavage mixture: trifluoroacetic acid:ethanedithiol:thioanisole:water:phenol (40:1:2:2:3). After cleaving for 2 hours, the peptides may be precipitated in cold methyl-t-butyl-ether. The peptide pellets may then be dissolved in water containing 0.1% trifluoroacetic acid (TFA) and lyophilized prior to purification by C18 reverse phase HPLC. A gradient of 0%-60% acetonitrile (containing 0.1% TFA) in water (containing 0.1% TFA) may be used to elute the peptides. Following lyophilization of the pure fractions, the peptides may be characterized using electrospray or other types of mass spectrometry and by amino acid analysis.

EXAMPLE 5

FURTHER ISOLATION AND CHARACTERIZATION OF PROSTATE-SPECIFIC POLYPEPTIDES BY PCR-BASED SUBTRACTION

5 A cDNA library generated from prostate primary tumor mRNA as described above was subtracted with cDNA from normal prostate. The subtraction was performed using a PCR-based protocol (Clontech), which was modified to generate larger fragments. Within this protocol, tester and driver double stranded cDNA were separately digested with
10 Sall and StuI). This digestion resulted in an average cDNA size of 600 bp, rather than the average size of 300 bp that results from digestion with RsaI according to the Clontech protocol. This modification did not affect the subtraction efficiency. Two tester populations were then created with different adapters, and the driver library remained without adapters.

15 The tester and driver libraries were then hybridized using excess driver cDNA. In the first hybridization step, driver was separately hybridized with each of the two tester cDNA populations. This resulted in populations of (a) unhybridized tester cDNAs, (b) tester cDNAs hybridized to other tester cDNAs, (c) tester cDNAs hybridized to driver cDNAs and (d) unhybridized driver cDNAs. The two separate hybridization
20 reactions were then combined, and rehybridized in the presence of additional denatured driver cDNA. Following this second hybridization, in addition to populations (a) through (d), a fifth population (e) was generated in which tester cDNA with one adapter hybridized to tester cDNA with the second adapter. Accordingly, the second hybridization step resulted in enrichment of differentially expressed sequences which could be used as
25 templates for PCR amplification with adaptor-specific primers.

 The ends were then filled in, and PCR amplification was performed using adaptor-specific primers. Only population (e), which contained tester cDNA that did not hybridize to driver cDNA, was amplified exponentially. A second PCR amplification step

was then performed, to reduce background and further enrich differentially expressed sequences.

This PCR-based subtraction technique normalizes differentially expressed cDNAs so that rare transcripts that are overexpressed in prostate tumor tissue may be recoverable. Such transcripts would be difficult to recover by traditional subtraction methods.

In addition to genes known to be overexpressed in prostate tumor, seventy-seven further clones were identified. Sequences of these partial cDNAs are provided in SEQ ID NO: 29 to 305. Most of these clones had no significant homology to database sequences. Exceptions were JPTPN23 (SEQ ID NO: 231; similarity to pig valosin-containing protein), JPTPN30 (SEQ ID NO: 234; similarity to rat mRNA for proteasome subunit), JPTPN45 (SEQ ID NO: 243; similarity to rat *norvegicus* cytosolic NADP-dependent isocitrate dehydrogenase), JPTPN46 (SEQ ID NO: 244; similarity to human subclone H8 4 d4 DNA sequence), JP1D6 (SEQ ID NO: 265; similarity to *G. gallus* dynein light chain-A), JP8D6 (SEQ ID NO: 288; similarity to human BAC clone RG016J04), JP8F5 (SEQ ID NO: 289; similarity to human subclone H8 3 b5 DNA sequence), and JP8E9 (SEQ ID NO: 299; similarity to human Alu sequence).

Additional studies using the PCR-based subtraction library consisting of a prostate tumor pool subtracted against a normal prostate pool (referred to as PT-PN PCR subtraction) yielded three additional clones. Comparison of the cDNA sequences of these clones with the most recent release of GenBank revealed no significant homologies to the two clones referred to as P715P and P767P (SEQ ID NO: 312 and 314). The remaining clone was found to show some homology to the known gene KIAA0056 (SEQ ID NO: 318). Using microarray analysis to measure mRNA expression levels in various tissues, all three clones were found to be over-expressed in prostate tumors and BPH tissues. Specifically, clone P715P was over-expressed in most prostate tumors and BPH tissues by a factor of three or greater, with elevated expression seen in the majority of normal prostate samples and in fetal tissue, but negative to low expression in all other normal tissues. Clone P767P was over-expressed in several prostate tumors and BPH tissues, with

moderate expression levels in half of the normal prostate samples, and background to low expression in all other normal tissues tested.

Further analysis, by microarray as described above, of the PT-PN PCR subtraction library and of a DNA subtraction library containing cDNA from prostate tumor subtracted with a pool of normal tissue cDNAs, led to the isolation of 27 additional clones (SEQ ID NO: 340-365 and 381) which were determined to be over-expressed in prostate tumor. The clones of SEQ ID NO: 341, 342, 345, 347, 348, 349, 351, 355-359, 361, 362 and 364 were also found to be expressed in normal prostate. Expression of all 26 clones in a variety of normal tissues was found to be low or undetectable, with the exception of P544S (SEQ ID NO: 356) which was found to be expressed in small intestine. Of the 26 clones, 11 (SEQ ID NO: 340-349 and 362) were found to show some homology to previously identified sequences. No significant homologies were found to the clones of SEQ ID NO: 350, 351, 353-361, and 363-365.

Comparison of the sequence of SEQ ID NO: 362 with sequences in the GenBank and GeneSeq DNA databases showed that this clone (referred to as P788P) is identical to GeneSeq Accession No. X27262, which encodes a protein found in the GeneSeq protein Accession No. Y00931. The full length cDNA sequence of P788P is shown in Figure 12A (SEQ ID NO: 777), with the corresponding predicted amino acid being shown in Figure 12B (SEQ ID NO: 778). Subsequently, a full-length cDNA sequence for P788P that contains polymorphisms not found in the sequence of SEQ ID NO: 779, was cloned multiple times by PCR amplification from cDNA prepared from several RNA templates from three individuals. This determined cDNA sequence of this polymorphic variant of P788P is provided in SEQ ID NO: 779, with the corresponding amino acid sequence being provided in SEQ ID NO: 780. The sequence of SEQ ID NO: 780 differs from that of SEQ ID NO: 778 by six amino acid residues. The P788P protein has 7 potential transmembrane domains at the C-terminal portion and is predicted to be a plasma membrane protein with an extracellular N-terminal region.

Further studies on the clone of SEQ ID NO: 352 (referred to as P790P) led to the isolation of the full-length cDNA sequence of SEQ ID NO: 526. The corresponding

predicted amino acid is provided in SEQ ID NO: 527. Data from two quantitative PCR experiments indicated that P790P is over-expressed in 11/15 tested prostate tumor samples and is expressed at low levels in spinal cord, with no expression being seen in all other normal samples tested. Data from further PCR experiments and microarray experiments

5 showed over-expression in normal prostate and prostate tumor with little or no expression in other tissues tested. P790P was subsequently found to show significant homology to a previously identified G-protein coupled prostate tissue receptor.

Additional studies on the clone of SEQ ID NO: 354 (referred to as P776P) led to the isolation of an extended cDNA sequence, provided in SEQ ID NO: 569. The

10 determined cDNA sequences of three additional splice variants of P776P are provided in SEQ ID NO: 570-572. The amino acid sequences encoded by two predicted open reading frames (ORFs) contained within SEQ ID NO: 570, one predicted ORF contained within SEQ ID NO: 571, and 11 predicted ORFs contained within SEQ ID NO: 569, are provided in SEQ ID NO: 573-586, respectively.

15 Comparison of the cDNA sequences for the clones P767P (SEQ ID NO: 314) and P777P (SEQ ID NO: 350) with sequences in the GenBank human EST database showed that the two clones matched many EST sequences in common, suggesting that P767P and P777P may represent the same gene. A DNA consensus sequence derived from a DNA sequence alignment of P767P, P777P and multiple EST clones is provided in

20 SEQ ID NO: 587. The amino acid sequences encoded by three putative ORFs located within SEQ ID NO: 587 are provided in SEQ ID NO: 588-590.

EXAMPLE 6

PEPTIDE PRIMING OF MICE AND PROPAGATION OF CTL LINES

25

6.1. This Example illustrates the preparation of a CTL cell line specific for cells expressing the P502S gene.

Mice expressing the transgene for human HLA A2Kb (provided by Dr L. Sherman, The Scripps Research Institute, La Jolla, CA) were immunized with P2S#12

peptide (VLGWVAEL; SEQ ID NO: 306), which is derived from the P502S gene (also referred to herein as J1-17, SEQ ID NO: 8), as described by Theobald et al., *Proc. Natl. Acad. Sci. USA* 92:11993-11997, 1995 with the following modifications. Mice were immunized with 100µg of P2S#12 and 120µg of an I-A^b binding peptide derived from hepatitis B Virus protein emulsified in incomplete Freund's adjuvant. Three weeks later these mice were sacrificed and using a nylon mesh single cell suspensions prepared. Cells were then resuspended at 6×10^6 cells/ml in complete media (RPMI-1640; Gibco BRL, Gaithersburg, MD) containing 10% FCS, 2mM Glutamine (Gibco BRL), sodium pyruvate (Gibco BRL), non-essential amino acids (Gibco BRL), 2×10^{-5} M 2-mercaptoethanol, 50U/ml penicillin and streptomycin, and cultured in the presence of irradiated (3000 rads) P2S#12-pulsed (5mg/ml P2S#12 and 10mg/ml β 2-microglobulin) LPS blasts (A2 transgenic spleens cells cultured in the presence of 7µg/ml dextran sulfate and 25µg/ml LPS for 3 days). Six days later, cells (5×10^5 /ml) were restimulated with 2.5×10^6 /ml peptide pulsed irradiated (20,000 rads) EL4A2Kb cells (Sherman et al, *Science* 258:815-818, 1992) and 3×10^6 /ml A2 transgenic spleen feeder cells. Cells were cultured in the presence of 20U/ml IL-2. Cells continued to be restimulated on a weekly basis as described, in preparation for cloning the line.

P2S#12 line was cloned by limiting dilution analysis with peptide pulsed EL4 A2Kb tumor cells (1×10^4 cells/ well) as stimulators and A2 transgenic spleen cells as feeders (5×10^5 cells/ well) grown in the presence of 30U/ml IL-2. On day 14, cells were restimulated as before. On day 21, clones that were growing were isolated and maintained in culture. Several of these clones demonstrated significantly higher reactivity (lysis) against human fibroblasts (HLA A2Kb expressing) transduced with P502S than against control fibroblasts. An example is presented in Figure 1.

This data indicates that P2S #12 represents a naturally processed epitope of the P502S protein that is expressed in the context of the human HLA A2Kb molecule.

6.2. This Example illustrates the preparation of murine CTL lines and CTL clones specific for cells expressing the P501S gene.

This series of experiments were performed similarly to that described above.

5 Mice were immunized with the P1S#10 peptide (SEQ ID NO: 337), which is derived from the P501S gene (also referred to herein as L1-12, SEQ ID NO: 110). The P1S#10 peptide was derived by analysis of the predicted polypeptide sequence for P501S for potential HLA-A2 binding sequences as defined by published HLA-A2 binding motifs (Parker, KC, *et al*, *J. Immunol.*, 152:163, 1994). P1S#10 peptide was synthesized as described in
10 Example 4, and empirically tested for HLA-A2 binding using a T cell based competition assay. Predicted A2 binding peptides were tested for their ability to compete HLA-A2 specific peptide presentation to an HLA-A2 restricted CTL clone (D150M58), which is specific for the HLA-A2 binding influenza matrix peptide fluM58. D150M58 CTL secretes TNF in response to self-presentation of peptide fluM58. In the competition assay,
15 test peptides at 100-200 µg/ml were added to cultures of D150M58 CTL in order to bind HLA-A2 on the CTL. After thirty minutes, CTL cultured with test peptides, or control peptides, were tested for their antigen dose response to the fluM58 peptide in a standard TNF bioassay. As shown in Figure 3, peptide P1S#10 competes HLA-A2 restricted presentation of fluM58, demonstrating that peptide P1S#10 binds HLA-A2.

20 Mice expressing the transgene for human HLA A2Kb were immunized as described by Theobald et al. (*Proc. Natl. Acad. Sci. USA* 92:11993-11997, 1995) with the following modifications. Mice were immunized with 62.5µg of P1S #10 and 120µg of an I-A^b binding peptide derived from Hepatitis B Virus protein emulsified in incomplete Freund's adjuvant. Three weeks later these mice were sacrificed and single cell
25 suspensions prepared using a nylon mesh. Cells were then resuspended at 6×10^6 cells/ml in complete media (as described above) and cultured in the presence of irradiated (3000 rads) P1S#10-pulsed (2µg/ml P1S#10 and 10mg/ml β2-microglobulin) LPS blasts (A2 transgenic spleens cells cultured in the presence of 7µg/ml dextran sulfate and 25µg/ml LPS for 3 days). Six days later cells (5×10^5 /ml) were restimulated with 2.5×10^6 /ml

peptide-pulsed irradiated (20,000 rads) EL4A2Kb cells, as described above, and 3×10^6 /ml A2 transgenic spleen feeder cells. Cells were cultured in the presence of 20 U/ml IL-2. Cells were restimulated on a weekly basis in preparation for cloning. After three rounds of *in vitro* stimulations, one line was generated that recognized P1S#10-pulsed Jurkat A2Kb targets and P501S-transduced Jurkat targets as shown in Figure 4.

A P1S#10-specific CTL line was cloned by limiting dilution analysis with peptide pulsed EL4 A2Kb tumor cells (1×10^4 cells/ well) as stimulators and A2 transgenic spleen cells as feeders (5×10^5 cells/ well) grown in the presence of 30U/ml IL-2. On day 14, cells were restimulated as before. On day 21, viable clones were isolated and maintained in culture. As shown in Figure 5, five of these clones demonstrated specific cytolytic reactivity against P501S-transduced Jurkat A2Kb targets. This data indicates that P1S#10 represents a naturally processed epitope of the P501S protein that is expressed in the context of the human HLA-A2.1 molecule.

EXAMPLE 7

PRIMING OF CTL *IN VIVO* USING NAKED DNA IMMUNIZATION

WITH A PROSTATE ANTIGEN

The prostate-specific antigen L1-12, as described above, is also referred to as P501S. HLA A2Kb Tg mice (provided by Dr L. Sherman, The Scripps Research Institute, La Jolla, CA) were immunized with 100 μ g P501S in the vector VR1012 either intramuscularly or intradermally. The mice were immunized three times, with a two week interval between immunizations. Two weeks after the last immunization, immune spleen cells were cultured with Jurkat A2Kb-P501S transduced stimulator cells. CTL lines were stimulated weekly. After two weeks of *in vitro* stimulation, CTL activity was assessed against P501S transduced targets. Two out of 8 mice developed strong anti-P501S CTL responses. These results demonstrate that P501S contains at least one naturally processed HLA-A2-restricted CTL epitope.

EXAMPLE 8

ABILITY OF HUMAN T CELLS TO RECOGNIZE PROSTATE-SPECIFIC POLYPEPTIDES

This Example illustrates the ability of T cells specific for a prostate tumor
 5 polypeptide to recognize human tumor.

Human CD8⁺ T cells were primed *in vitro* to the P2S-12 peptide (SEQ ID NO: 306) derived from P502S (also referred to as J1-17) using dendritic cells according to the protocol of Van Tsai et al. (*Critical Reviews in Immunology* 18:65-75, 1998). The resulting CD8⁺ T cell microcultures were tested for their ability to recognize the P2S-12
 10 peptide presented by autologous fibroblasts or fibroblasts which were transduced to express the P502S gene in a γ -interferon ELISPOT assay (*see* Lalvani et al., *J. Exp. Med.* 186:859-865, 1997). Briefly, titrating numbers of T cells were assayed in duplicate on 10⁴ fibroblasts in the presence of 3 μ g/ml human β_2 -microglobulin and 1 μ g/ml P2S-12 peptide or control E75 peptide. In addition, T cells were simultaneously assayed on autologous
 15 fibroblasts transduced with the P502S gene or as a control, fibroblasts transduced with HER-2/*neu*. Prior to the assay, the fibroblasts were treated with 10 ng/ml γ -interferon for 48 hours to upregulate class I MHC expression. One of the microcultures (#5) demonstrated strong recognition of both peptide pulsed fibroblasts as well as transduced fibroblasts in a γ -interferon ELISPOT assay. Figure 2A demonstrates that there was a
 20 strong increase in the number of γ -interferon spots with increasing numbers of T cells on fibroblasts pulsed with the P2S-12 peptide (solid bars) but not with the control E75 peptide (open bars). This shows the ability of these T cells to specifically recognize the P2S-12 peptide. As shown in Figure 2B, this microculture also demonstrated an increase in the number of γ -interferon spots with increasing numbers of T cells on fibroblasts transduced
 25 to express the P502S gene but not the HER-2/*neu* gene. These results provide additional confirmatory evidence that the P2S-12 peptide is a naturally processed epitope of the P502S protein. Furthermore, this also demonstrates that there exists in the human T cell repertoire, high affinity T cells which are capable of recognizing this epitope. These T cells should also be capable of recognizing human tumors which express the P502S gene.

EXAMPLE 9
ELICITATION OF PROSTATE ANTIGEN-SPECIFIC CTL RESPONSES
IN HUMAN BLOOD

5

This Example illustrates the ability of a prostate-specific antigen to elicit a CTL response in blood of normal humans.

Autologous dendritic cells (DC) were differentiated from monocyte cultures derived from PBMC of normal donors by growth for five days in RPMI medium containing

10 10% human serum, 50 ng/ml GM-CSF and 30 ng/ml IL-4. Following culture, DC were infected overnight with recombinant P501S-expressing vaccinia virus at an M.O.I. of 5 and matured for 8 hours by the addition of 2 micrograms/ml CD40 ligand. Virus was inactivated by UV irradiation, CD8⁺ cells were isolated by positive selection using magnetic beads, and priming cultures were initiated in 24-well plates. Following five

15 stimulation cycles using autologous fibroblasts retrovirally transduced to express P501S and CD80, CD8⁺ lines were identified that specifically produced interferon-gamma when stimulated with autologous P501S-transduced fibroblasts. The P501S-specific activity of cell line 3A-1 could be maintained following additional stimulation cycles on autologous B-LCL transduced with P501S. Line 3A-1 was shown to specifically recognize autologous

20 B-LCL transduced to express P501S, but not EGFP-transduced autologous B-LCL, as measured by cytotoxicity assays (⁵¹Cr release) and interferon-gamma production (Interferon-gamma Elispot; *see above and Lalvani et al., J. Exp. Med.* 186:859-865, 1997). The results of these assays are presented in Figures 6A and 6B.

EXAMPLE 10

IDENTIFICATION OF A NATURALLY PROCESSED CTL EPITOPE CONTAINED WITHIN THE
PROSTATE-SPECIFIC ANTIGEN P703P

5 The 9-mer peptide p5 (SEQ ID NO: 338) was derived from the P703P antigen (also referred to as P20). The p5 peptide is immunogenic in human HLA-A2 donors and is a naturally processed epitope. Antigen specific human CD8+ T cells can be primed following repeated *in vitro* stimulations with monocytes pulsed with p5 peptide. These CTL specifically recognize p5-pulsed and P703P-transduced target cells in both
10 ELISPOT (as described above) and chromium release assays. Additionally, immunization of HLA-A2Kb transgenic mice with p5 leads to the generation of CTL lines which recognize a variety of HLA-A2Kb or HLA-A2 transduced target cells expressing P703P.

 Initial studies demonstrating that p5 is a naturally processed epitope were done using HLA-A2Kb transgenic mice. HLA-A2Kb transgenic mice were immunized
15 subcutaneously in the footpad with 100 µg of p5 peptide together with 140 µg of hepatitis B virus core peptide (a Th peptide) in Freund's incomplete adjuvant. Three weeks post immunization, spleen cells from immunized mice were stimulated *in vitro* with peptide-pulsed LPS blasts. CTL activity was assessed by chromium release assay five days after primary *in vitro* stimulation. Retrovirally transduced cells expressing the control antigen
20 P703P and HLA-A2Kb were used as targets. CTL lines that specifically recognized both p5-pulsed targets as well as P703P-expressing targets were identified.

 Human *in vitro* priming experiments demonstrated that the p5 peptide is immunogenic in humans. Dendritic cells (DC) were differentiated from monocyte cultures derived from PBMC of normal human donors by culturing for five days in RPMI medium
25 containing 10% human serum, 50 ng/ml human GM-CSF and 30 ng/ml human IL-4. Following culture, the DC were pulsed with 1 µg/ml p5 peptide and cultured with CD8+ T cell enriched PBMC. CTL lines were restimulated on a weekly basis with p5-pulsed monocytes. Five to six weeks after initiation of the CTL cultures, CTL recognition of p5-

pulsed target cells was demonstrated. CTL were additionally shown to recognize human cells transduced to express P703P, demonstrating that p5 is a naturally processed epitope.

Studies identifying a further peptide epitope (referred to as peptide 4) derived from the prostate tumor-specific antigen P703P that is capable of being recognized by CD4 T cells on the surface of cells in the context of HLA class II molecules were carried out as follows. The amino acid sequence for peptide 4 is provided in SEQ ID NO: 781, with the corresponding cDNA sequence being provided in SEQ ID NO: 782.

Twenty 15-mer peptides overlapping by 10 amino acids and derived from the carboxy-terminal fragment of P703P were generated using standard procedures. Dendritic cells (DC) were derived from PBMC of a normal female donor using GM-CSF and IL-4 by standard protocols. CD4 T cells were generated from the same donor as the DC using MACS beads and negative selection. DC were pulsed overnight with pools of the 15-mer peptides, with each peptide at a final concentration of 0.25 microgram/ml. Pulsed DC were washed and plated at 1×10^4 cells/well of 96-well V-bottom plates and purified CD4 T cells were added at 1×10^5 /well. Cultures were supplemented with 60 ng/ml IL-6 and 10 ng/ml IL-12 and incubated at 37 °C. Cultures were restimulated as above on a weekly basis using DC generated and pulsed as above as antigen presenting cells, supplemented with 5 ng/ml IL-7 and 10 u/ml IL-2. Following 4 *in vitro* stimulation cycles, 96 lines (each line corresponding to one well) were tested for specific proliferation and cytokine production in response to the stimulating pools with an irrelevant pool of peptides derived from mammaglobin being used as a control.

One line (referred to as 1-F9) was identified from pool #1 that demonstrated specific proliferation (measured by 3H proliferation assays) and cytokine production (measured by interferon-gamma ELISA assays) in response to pool #1 of P703P peptides. This line was further tested for specific recognition of the peptide pool, specific recognition of individual peptides in the pool, and in HLA mismatch analyses to identify the relevant restricting allele. Line 1-F9 was found to specifically proliferate and produce interferon-gamma in response to peptide pool #1, and also to peptide 4 (SEQ ID NO: 781). Peptide 4 corresponds to amino acids 126-140 of SEQ ID NO: 327. Peptide titration experiments were conducted to assess the sensitivity of line 1-F9 for the specific peptide. The line was

found to specifically respond to peptide 4 at concentrations as low as 0.25 ng/ml, indicating that the T cells are very sensitive and therefore likely to have high affinity for the epitope.

To determine the HLA restriction of the P703P response, a panel of antigen presenting cells (APC) was generated that was partially matched with the donor used to generate the T cells. The APC were pulsed with the peptide and used in proliferation and cytokine assays together with line 1-F9. APC matched with the donor at HLA-DRB0701 and HLA-DQB02 alleles were able to present the peptide to the T cells, indicating that the P703P-specific response is restricted to one of these alleles.

Antibody blocking assays were utilized to determine if the restricting allele was HLA-DR0701 or HLA-DQ02. The anti-HLA-DR blocking antibody L243 or an irrelevant isotype matched IgG2a were added to T cells and APC cultures pulsed with the peptide RMPTVLQCVNVS VVS (SEQ ID NO: 781) at 250 ng/ml. Standard interferon-gamma and proliferation assays were performed. Whereas the control antibody had no effect on the ability of the T cells to recognize peptide-pulsed APC, in both assays the anti-HLA-DR antibody completely blocked the ability of the T cells to specifically recognize peptide-pulsed APC.

To determine if the peptide epitope RMPTVLQCVNVS VVS (SEQ ID NO: 781) was naturally processed, the ability of line 1-F9 to recognize APC pulsed with recombinant P703P protein was examined. For these experiments a number of recombinant P703P sources were utilized; *E. coli*-derived P703P, Pichia-derived P703P and baculovirus-derived P703P. Irrelevant protein controls used were *E. coli*-derived L3E (a lung-specific antigen) and baculovirus-derived mammaglobin. In interferon-gamma ELISA assays, line 1-F9 was able to efficiently recognize both *E. coli* forms of P703P as well as Pichia-derived recombinant P703P, while baculovirus-derived P703P was recognized less efficiently. Subsequent Western blot analysis revealed that the *E. coli* and Pichia P703P protein preparations were intact while the baculovirus P703P preparation was approximately 75% degraded. Thus, peptide RMPTVLQCVNVS VVS (SEQ ID NO: 781) from P703P is a naturally processed peptide epitope derived from P703P and presented to T cells in the context of HLA-DRB-0701

In further studies, twenty-four 15-mer peptides overlapping by 10 amino

acids and derived from the N-terminal fragment of P703P (corresponding to amino acids 27-154 of SEQ ID NO: 525) were generated by standard procedures and their ability to be recognized by CD4 cells was determined essentially as described above. DC were pulsed overnight with pools of the peptides with each peptide at a final concentration of 10 microgram/ml. A large number of individual CD4 T cell lines (65/480) demonstrated significant proliferation and cytokine release (IFN-gamma) in response to the P703P peptide pools but not to a control peptide pool. The CD4 T cell lines which demonstrated specific activity were restimulated on the appropriate pool of P703P peptides and reassayed on the individual peptides of each pool as well as a peptide dose titration of the pool of peptides in a IFN-gamma release assay and in a proliferation assay.

Sixteen immunogenic peptides were recognized by the T cells from the entire set of peptide antigens tested. The amino acid sequences of these peptides are provided in SEQ ID NO: 799-814, with the corresponding cDNA sequences being provided in SEQ ID NO: 783-798, respectively. In some cases the peptide reactivity of the T cell line could be mapped to a single peptide, however some could be mapped to more than one peptide in each pool. Those CD4 T cell lines that displayed a representative pattern of recognition from each peptide pool with a reasonable affinity for peptide were chosen for further analysis (I-1A, -6A; II-4C, -5E; III-6E, IV-4B, -3F, -9B, -10F, V-5B, -4D, and -10F). These CD4 T cells lines were restimulated on the appropriate individual peptide and reassayed on autologous DC pulsed with a truncated form of recombinant P703P protein made in *E. coli* (a.a. 96 - 254 of SEQ ID NO: 525), full-length P703P made in the baculovirus expression system, and a fusion between influenza virus NS1 and P703P made in *E. coli*. Of the T cell lines tested, line I-1A recognized specifically the truncated form of P703P (*E. coli*) but no other recombinant form of P703P. This line also recognized the peptide used to elicit the T cells. Line 2-4C recognized the truncated form of P703P (*E. coli*) and the full length form of P703P made in baculovirus, as well as peptide. The remaining T cell lines tested were either peptide-specific only (II-5E, II-6F, IV-4B, IV-3F, IV-9B, IV-10F, V-5B and V-4D) or were non-responsive to any antigen tested (V-10F). These results demonstrate that the peptide sequence RPLLANDLMLIKLDE (SEQ ID NO: 814; corresponding to a.a. 110-124 of SEQ ID NO: 525) recognized by the T cell line I-1A,

and the peptide sequences SVSESDTIRSISIAS (SEQ ID NO: 811; corresponding to a.a. 125-139 of SEQ ID NO: 525) and ISIASQCPTAGNSCL (SEQ ID NO: 810; corresponding to a.a. 135-149 of SEQ ID NO: 525) recognized by the T cell line II-4C may be naturally processed epitopes of the P703P protein.

5

EXAMPLE 11

EXPRESSION OF A BREAST TUMOR-DERIVED ANTIGEN

IN PROSTATE

10 Isolation of the antigen B305D from breast tumor by differential display is described in US Patent Application No. 08/700,014, filed August 20, 1996. Several different splice forms of this antigen were isolated. The determined cDNA sequences for these splice forms are provided in SEQ ID NO: 366-375, with the predicted amino acid sequences corresponding to the sequences of SEQ ID NO: 292, 298 and 301-303 being
15 provided in SEQ ID NO: 299-306, respectively. In further studies, a splice variant of the cDNA sequence of SEQ ID NO: 366 was isolated which was found to contain an additional guanine residue at position 884 (SEQ ID NO: 530), leading to a frameshift in the open reading frame. The determined DNA sequence of this ORF is provided in SEQ ID NO: 531. This frameshift generates a protein sequence (provided in SEQ ID NO: 532) of 293
20 amino acids that contains the C-terminal domain common to the other isoforms of B305D but that differs in the N-terminal region.

The expression levels of B305D in a variety of tumor and normal tissues were examined by real time PCR and by Northern analysis. The results indicated that B305D is highly expressed in breast tumor, prostate tumor, normal prostate and normal
25 testes, with expression being low or undetectable in all other tissues examined (colon tumor, lung tumor, ovary tumor, and normal bone marrow, colon, kidney, liver, lung, ovary, skin, small intestine, stomach). Using real-time PCR on a panel of prostate tumors, expression of B305D in prostate tumors was shown to increase with increasing Gleason grade, demonstrating that expression of B305D increases as prostate cancer progresses.

EXAMPLE 12

GENERATION OF HUMAN CTL *IN VITRO* USING WHOLE GENE PRIMING AND STIMULATION
TECHNIQUES WITH THE PROSTATE-SPECIFIC ANTIGEN P501S

5

Using *in vitro* whole-gene priming with P501S-vaccinia infected DC (see, for example, Yee et al, *The Journal of Immunology*, 157(9):4079-86, 1996), human CTL lines were derived that specifically recognize autologous fibroblasts transduced with P501S (also known as L1-12), as determined by interferon- γ ELISPOT analysis as described

10 above. Using a panel of HLA-mismatched B-LCL lines transduced with P501S, these CTL lines were shown to be likely restricted to HLAB class I allele. Specifically, dendritic cells (DC) were differentiated from monocyte cultures derived from PBMC of normal human donors by growing for five days in RPMI medium containing 10% human serum, 50 ng/ml human GM-CSF and 30 ng/ml human IL-4. Following culture, DC were infected

15 overnight with recombinant P501S vaccinia virus at a multiplicity of infection (M.O.I) of five, and matured overnight by the addition of 3 μ g/ml CD40 ligand. Virus was inactivated by UV irradiation. CD8⁺ T cells were isolated using a magnetic bead system, and priming cultures were initiated using standard culture techniques. Cultures were restimulated every 7-10 days using autologous primary fibroblasts retrovirally transduced with P501S and

20 CD80. Following four stimulation cycles, CD8⁺ T cell lines were identified that specifically produced interferon- γ when stimulated with P501S and CD80-transduced autologous fibroblasts. A panel of HLA-mismatched B-LCL lines transduced with P501S were generated to define the restriction allele of the response. By measuring interferon- γ in an ELISPOT assay, the P501S specific response was shown to be likely restricted by HLA

25 B alleles. These results demonstrate that a CD8⁺ CTL response to P501S can be elicited.

To identify the epitope(s) recognized, cDNA encoding P501S was fragmented by various restriction digests, and sub-cloned into the retroviral expression vector pBIB-KS. Retroviral supernatants were generated by transfection of the helper packaging line Phoenix-Ampho. Supernatants were then used to transduce Jurkat/A2Kb

cells for CTL screening. CTL were screened in IFN-gamma ELISPOT assays against these A2Kb targets transduced with the “library” of P501S fragments. Initial positive fragments P501S/H3 and P501S/F2 were sequenced and found to encode amino acids 106-553 and amino acids 136-547, respectively, of SEQ ID NO: 113. A truncation of H3 was made to
 5 encode amino acid residues 106-351 of SEQ ID NO: 113, which was unable to stimulate the CTL, thus localizing the epitope to amino acid residues 351-547. Additional fragments encoding amino acids 1-472 (Fragment A) and amino acids 1-351 (Fragment B) were also constructed. Fragment A but not Fragment B stimulated the CTL thus localizing the epitope to amino acid residues 351-472. Overlapping 20-mer and 18-mer peptides
 10 representing this region were tested by pulsing Jurkat/A2Kb cells versus CTL in an IFN-gamma assay. Only peptides P501S-369(20) and P501S-369(18) stimulated the CTL. Nine-mer and 10-mer peptides representing this region were synthesized and similarly tested. Peptide P501S-370 (SEQ ID NO: 539) was the minimal 9-mer giving a strong response. Peptide P501S-376 (SEQ ID NO: 540) also gave a weak response, suggesting
 15 that it might represent a cross-reactive epitope.

In subsequent studies, the ability of primary human B cells transduced with P501S to prime MHC class I-restricted, P501S-specific, autologous CD8 T cells was examined. Primary B cells were derived from PBMC of a homozygous HLA-A2 donor by culture in CD40 ligand and IL-4, transduced at high frequency with recombinant P501S in
 20 the vector pBIB, and selected with blastocidin-S. For *in vitro* priming, purified CD8+ T cells were cultured with autologous CD40 ligand + IL-4 derived, P501S-transduced B cells in a 96-well microculture format. These CTL microcultures were re-stimulated with P501S-transduced B cells and then assayed for specificity. Following this initial screen, microcultures with significant signal above background were cloned on autologous EBV-
 25 transformed B cells (BLCL), also transduced with P501S. Using IFN-gamma ELISPOT for detection, several of these CD8 T cell clones were found to be specific for P501S, as demonstrated by reactivity to BLCL/P501S but not BLCL transduced with control antigen. It was further demonstrated that the anti-P501S CD8 T cell specificity is HLA-A2-restricted. First, antibody blocking experiments with anti-HLA-A,B,C monoclonal

antibody (W6.32), anti-HLA-B,C monoclonal antibody (B1.23.2) and a control monoclonal antibody showed that only the anti-HLA-A,B,C antibody blocked recognition of P501S-expressing autologous BLCL. Secondly, the anti-P501S CTL also recognized an HLA-A2 matched, heterologous BLCL transduced with P501S, but not the corresponding EGFP transduced control BLCL.

A naturally processed, CD8, class I-restricted peptide epitope of P501S was identified as follows. Dendritic Cells (DC) were isolated by Percol gradient followed by differential adherence, and cultured for 5 days in the presence of RPMI medium containing 1% human serum, 50ng/ml GM-CSF and 30ng/ml IL-4. Following culture, DC were infected for 24 hours with P501S-expressing adenovirus at an MOI of 10 and matured for an additional 24 hours by the addition of 2ug/ml CD40 ligand. CD8 cells were enriched for by the subtraction of CD4+, CD14+ and CD16+ populations from PBMC with magnetic beads. Priming cultures containing 10,000 P501S-expressing DC and 100,000 CD8+ T cells per well were set up in 96-well V-bottom plates with RPMI containing 10% human serum, 5ng/ml IL-12 and 10ng/ml IL-6. Cultures were stimulated every 7 days using autologous fibroblasts retrovirally transduced to express P501S and CD80, and were treated with IFN-gamma for 48-72 hours to upregulate MHC Class I expression. 10u/ml IL-2 was added at the time of stimulation and on days 2 and 5 following stimulation. Following 4 stimulation cycles, one P501S-specific CD8+ T cell line (referred to as 2A2) was identified that produced IFN-gamma in response to IFN-gamma-treated P501S/CD80 expressing autologous fibroblasts, but not in response to IFN-gamma-treated P703P/CD80 expressing autologous fibroblasts in a γ -IFN Elispot assay. Line 2A2 was cloned in 96-well plates with 0.5 cell/well or 2 cells/well in the presence of 75,000 PBMC/well, 10,000 B-LCL/well, 30ng/ml OKT3 and 50u/ml IL-2. Twelve clones were isolated that showed strong P501S specificity in response to transduced fibroblasts.

Fluorescence activated cell sorting (FACS) analysis was performed on P501S-specific clones using CD3-, CD4- and CD8-specific antibodies conjugated to PercP, FITC and PE respectively. Consistent with the use of CD8 enriched T cells in the priming cultures, P5401S-specific clones were determined to be CD3+, CD8+ and CD4-.

To identify the relevant P501S epitope recognized by P501S specific CTL,

pools of 18-20 mer or 30-mer peptides that spanned the majority of the amino acid
 sequence of P501S were loaded onto autologous B-LCL and tested in γ -IFN Elispot assays
 for the ability to stimulate two P501S-specific CTL clones, referred to as 4E5 and 4E7.
 One pool, composed of five 18-20 mer peptides that spanned amino acids 411-486 of
 5 P501S (SEQ ID NO: 113), was found to be recognized by both P501S-specific clones. To
 identify the specific 18-20 mer peptide recognized by the clones, each of the 18-20 mer
 peptides that comprised the positive pool were tested individually in γ -IFN Elispot assays
 for the ability to stimulate the two P501S-specific CTL clones, 4E5 and 4E7. Both 4E5
 and 4E7 specifically recognized one 20-mer peptide (SEQ ID NO: 853; cDNA sequence
 10 provided in SEQ ID NO: 854) that spanned amino acids 453-472 of P501S. Since the
 minimal epitope recognized by CD8⁺ T cells is almost always either a 9 or 10-mer peptide
 sequence, 10-mer peptides that spanned the entire sequence of SEQ ID NO: 853 were
 synthesized that differed by 1 amino acid. Each of these 10-mer peptides was tested for the
 ability to stimulate two P501S-specific clones, (referred to as 1D5 and 1E12). One 10-mer
 15 peptide (SEQ ID NO: 855; cDNA sequence provided in SEQ ID NO: 856) was identified
 that specifically stimulated the P501S-specific clones. This epitope spans amino acids 463-
 472 of P501S. This sequence defines a minimal 10-mer epitope from P501S that can be
 naturally processed and to which CTL responses can be identified in normal PBMC. Thus,
 this epitope is a candidate for use as a vaccine moiety, and as a therapeutic and/or
 20 diagnostic reagent for prostate cancer.

To identify the class I restriction element for the P501S-derived sequence of
 SEQ ID NO: 855, HLA blocking and mismatch analyses were performed. In γ -IFN Elispot
 assays, the specific response of clones 4A7 and 4E5 to P501S-transduced autologous
 fibroblasts was blocked by pre-incubation with 25ug/ml W6/32 (pan-Class I blocking
 25 antibody) and B1.23.2 (HLA-B/C blocking antibody). These results demonstrate that the
 SEQ ID NO: 855-specific response is restricted to an HLA-B or HLA-C allele.

For the HLA mismatch analysis, autologous B-LCL (HLA-A1,A2,B8,B51,
 Cw1, Cw7) and heterologous B-LCL (HLA-A2,A3,B18,B51,Cw5,Cw14) that share the
 HLAB51 allele were pulsed for one hour with 20ug/ml of peptide of SEQ ID NO: 855,
 30 washed, and tested in γ -IFN Elispot assays for the ability to stimulate clones 4A7 and 4E5.

Antibody blocking assays with the B1.23.2 (HLA-B/C blocking antibody) were also performed. SEQ ID NO: 855-specific response was detected using both the autologous (D326) and heterologous (D107) B-LCL, and furthermore the responses were blocked by pre-incubation with 25ug/ml of B1.23.2 HLA-B/C blocking antibody. Together these

5 results demonstrate that the P501S-specific response to the peptide of SEQ ID NO: 855 is restricted to the HLA-B51 class I allele. Molecular cloning and sequence analysis of the HLA-B51 allele from D3326 revealed that the HLA-B51 subtype of D326 is HLA-B51011.

Based on the 10-mer P501S-derived epitope of SEQ ID NO: 855, two 9-mers with the sequences of SEQ ID NO: 857 and 858 were synthesized and tested in

10 Elispot assays for the ability to stimulate two P501S-specific CTL clones derived from line 2A2. The 10-mer peptide of SEQ ID NO: 855, as well as the 9-mer peptide of SEQ ID NO: 858, but not the 9-mer peptide of SEQ ID NO: 857, were capable of stimulating the P501S-specific CTL to produce IFN-gamma. These results demonstrate that the peptide of SEQ ID NO: 858 is a 9-mer P501S-derived epitope recognized by P501S-specific CTL.

15 The DNA sequence encoding the epitope of SEQ ID NO: 858 is provided in SEQ ID NO: 859.

To identify the class I restricting allele for the P501S-derived peptide of SEQ ID NO: 855 and 858 specific response, each of the HLA B and C alleles were cloned from the donor used in the *in vitro* priming experiment. Sequence analysis indicated that

20 the relevant alleles were HLA-B8, HLA-B51, HLA-Cw01 and HLA-Cw07. Each of these alleles were subcloned into an expression vector and co-transfected together with the P501S gene into VA-13 cells. Transfected VA-13 cells were then tested for the ability to specifically stimulate the P501S-specific CTL in ELISPOT assays. VA-13 cells transfected with P501S and HLA-B51 were capable of stimulating the P501S-specific CTL

25 to secrete gamma-IFN. VA-13 cells transfected with HLA-B51 alone or P501S + the other HLA-alleles were not capable of stimulating the P501S-specific CTL. These results demonstrate that the restricting allele for the P501S-specific response is the HLAB51 allele. Sequence analysis revealed that the subtype of the relevant restricting allele is HLA-B51011.

30 A naturally processed CD4 epitope of P501S was identified as follows.

CD4 cells specific for P501S were prepared as described above. A series of 16 overlapping peptides were synthesized that spanned approximately 50% of the amino terminal portion of the P501S gene (amino acids 1- 325 of SEQ ID NO: 113). For priming, peptides were combined into pools of 4 peptides, pulsed at 4 μ g/ml onto dendritic cells (DC) for 24 hours, with TNF-alpha. DC were then washed and mixed with negatively selected CD4+ T cells in 96 well U-bottom plates. Cultures were re-stimulated weekly on fresh DC loaded with peptide pools. Following a total of 4 stimulation cycles, cells were rested for an additional week and tested for specificity to APC pulsed with peptide pools using γ -IFN ELISA and proliferation assays. For these assays, adherent monocytes loaded with either the relevant peptide pool at 4ug/ml or an irrelevant peptide at μ g/ml were used as APC. T cell lines that demonstrated either specific cytokine secretion or proliferation were then tested for recognition of individual peptides that were present in the pool. T cell lines could be identified from pools A and B that recognized individual peptides from these pools.

FROM POOL A, LINES AD9 AND AE10 SPECIFICALLY RECOGNIZED PEPTIDE 1 (SEQ ID NO: 862), AND LINE AF5 RECOGNIZED PEPTIDE 39 (SEQ ID NO: 861). FROM POOL B, LINE BC6 COULD BE IDENTIFIED THAT RECOGNIZED PEPTIDE 58 (SEQ ID NO: 860). EACH OF THESE LINES WERE STIMULATED ON THE

5 SPECIFIC PEPTIDE AND TESTED FOR SPECIFIC RECOGNITION OF THE PEPTIDE IN A TITRATION ASSAY AS WELL AS CELL LYSATES GENERATED BY INFECTION OF HEK 293 CELLS WITH ADENOVIRUS EXPRESSING EITHER P501S OR AN IRRELEVANT ANTIGEN. FOR THESE ASSAYS, APC-ADHERENT MONOCYTES WERE PULSED WITH EITHER 10, 1, OR 0.1 μ G/ML INDIVIDUAL

10 P501S PEPTIDES, AND DC WERE PULSED OVERNIGHT WITH A 1:5 DILUTION OF ADENOVIRALLY INFECTED CELL LYSATES. LINES AD9, AE10 AND AF5 RETAINED SIGNIFICANT RECOGNITION OF THE RELEVANT P501S-DERIVED PEPTIDES EVEN AT 0.1 MG/ML. FURTHERMORE, LINE AD9 DEMONSTRATED SIGNIFICANT (8.1 FOLD STIMULATION INDEX) SPECIFIC ACTIVITY FOR

15 LYSATES FROM ADENOVIRUS-P501S INFECTED CELLS. THESE RESULTS DEMONSTRATE THAT HIGH AFFINITY CD4 T CELL LINES CAN BE GENERATED TOWARD P501S-DERIVED EPITOPES, AND THAT AT LEAST A SUBSET OF THESE T CELLS SPECIFIC FOR THE P501S DERIVED SEQUENCE OF SEQ ID NO: 862 ARE SPECIFIC FOR AN EPITOPE THAT IS NATURALLY

20 PROCESSED BY HUMAN CELLS. THE DNA SEQUENCES ENCODING THE AMINO ACID SEQUENCES OF SEQ ID NO: 860-862 ARE PROVIDED IN SEQ ID NO: 863-865, RESPECTIVELY.

EXAMPLE 13

IDENTIFICATION OF PROSTATE-SPECIFIC ANTIGENS

25 BY MICROARRAY ANALYSIS

This Example describes the isolation of certain prostate-specific polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library as described above was

30 screened using microarray analysis to identify clones that display at least a three fold over-

expression in prostate tumor and/or normal prostate tissue, as compared to non-prostate normal tissues (not including testis). 372 clones were identified, and 319 were successfully sequenced. Table I presents a summary of these clones, which are shown in SEQ ID NOs:385-400. Of these sequences SEQ ID NOs:386, 389, 390 and 392 correspond to
 5 novel genes, and SEQ ID NOs: 393 and 396 correspond to previously identified sequences. The others (SEQ ID NOs:385, 387, 388, 391, 394, 395 and 397-400) correspond to known sequences, as shown in Table I.

Table I

Summary of Prostate Tumor Antigens

Known Genes	Previously Identified Genes	Novel Genes
T-cell gamma chain	P504S	23379 (SEQ ID NO:389)
Kallikrein	P1000C	23399 (SEQ ID NO:392)
Vector	P501S	23320 (SEQ ID NO:386)
CGI-82 protein mRNA (23319; SEQ ID NO:385)	P503S	23381 (SEQ ID NO:390)
PSA	P510S	
Ald. 6 Dehyd.	P784P	
L-itol-2 dehydrogenase (23376; SEQ ID NO:388)	P502S	
Ets transcription factor PDEF (22672; SEQ ID NO:398)	P706P	
hTGR (22678; SEQ ID NO:399)	19142.2, bangur.seq (22621; SEQ ID NO:396)	
KIAA0295(22685; SEQ ID NO:400)	5566.1 Wang (23404; SEQ ID NO:393)	
Prostatic Acid Phosphatase(22655; SEQ ID NO:397)	P712P	
transglutaminase (22611; SEQ ID NO:395)	P778P	
HDLBP (23508; SEQ ID NO:394)		
CGI-69 Protein(23367; SEQ ID NO:387)		
KIAA0122(23383; SEQ ID NO:391)		
TEEG		

CGI-82 showed 4.06 fold over-expression in prostate tissues as compared to
5 other normal tissues tested. It was over-expressed in 43% of prostate tumors, 25% normal

prostate, not detected in other normal tissues tested. L-iditol-2 dehydrogenase showed 4.94 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 90% of prostate tumors, 100% of normal prostate, and not detected in other normal tissues tested. Ets transcription factor PDEF showed 5.55 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 47% prostate tumors, 25% normal prostate and not detected in other normal tissues tested. hTGR1 showed 9.11 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 63% of prostate tumors and is not detected in normal tissues tested including normal prostate. KIAA0295 showed 5.59 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 47% of prostate tumors, low to undetectable in normal tissues tested including normal prostate tissues. Prostatic acid phosphatase showed 9.14 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 67% of prostate tumors, 50% of normal prostate, and not detected in other normal tissues tested. Transglutaminase showed 14.84 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 30% of prostate tumors, 50% of normal prostate, and is not detected in other normal tissues tested. High density lipoprotein binding protein (HDLBP) showed 28.06 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 97% of prostate tumors, 75% of normal prostate, and is undetectable in all other normal tissues tested. CGI-69 showed 3.56 fold over-expression in prostate tissues as compared to other normal tissues tested. It is a low abundant gene, detected in more than 90% of prostate tumors, and in 75% normal prostate tissues. The expression of this gene in normal tissues was very low. KIAA0122 showed 4.24 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 57% of prostate tumors, it was undetectable in all normal tissues tested including normal prostate tissues. 19142.2 bangur showed 23.25 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 97% of prostate tumors and 100% of normal prostate. It was undetectable in other normal tissues tested. 5566.1 Wang showed 3.31 fold over-

expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 97% of prostate tumors, 75% normal prostate and was also over-expressed in normal bone marrow, pancreas, and activated PBMC. Novel clone 23379 (also referred to as P553S) showed 4.86 fold over-expression in prostate tissues as compared to other normal tissues tested. It was detectable in 97% of prostate tumors and 75% normal prostate and is undetectable in all other normal tissues tested. Novel clone 23399 showed 4.09 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 27% of prostate tumors and was undetectable in all normal tissues tested including normal prostate tissues. Novel clone 23320 showed 3.15 fold over-expression in prostate tissues as compared to other normal tissues tested. It was detectable in all prostate tumors and 50% of normal prostate tissues. It was also expressed in normal colon and trachea. Other normal tissues do not express this gene at high level.

Subsequent full-length cloning studies on P553S, using standard techniques, revealed that this clone is an incomplete spliced form of P501S. The determined cDNA sequences for four splice variants of P553S are provided in SEQ ID NO: 702-705. An amino acid sequence encoded by SEQ ID NO: 705 is provided in SEQ ID NO: 706. The cDNA sequence of SEQ ID NO: 702 was found to contain two open reading frames (ORFs). The amino acid sequences encoded by these two ORFs are provided in SEQ ID NO: 707 and 708.

EXAMPLE 14

IDENTIFICATION OF PROSTATE-SPECIFIC ANTIGENS

BY ELECTRONIC SUBTRACTION

This Example describes the use of an electronic subtraction technique to identify prostate-specific antigens.

Potential prostate-specific genes present in the GenBank human EST database were identified by electronic subtraction (similar to that described by Vasmatizis et al., *Proc. Natl. Acad. Sci. USA* 95:300-304, 1998). The sequences of EST clones

(43,482) derived from various prostate libraries were obtained from the GenBank public human EST database. Each prostate EST sequence was used as a query sequence in a BLASTN (National Center for Biotechnology Information) search against the human EST database. All matches considered identical (length of matching sequence >100 base pairs, density of identical matches over this region > 70%) were grouped (aligned) together in a cluster. Clusters containing more than 200 ESTs were discarded since they probably represented repetitive elements or highly expressed genes such as those for ribosomal proteins. If two or more clusters shared common ESTs, those clusters were grouped together into a “supercluster,” resulting in 4,345 prostate superclusters.

Records for the 479 human cDNA libraries represented in the GenBank release were downloaded to create a database of these cDNA library records. These 479 cDNA libraries were grouped into three groups: Plus (normal prostate and prostate tumor libraries, and breast cell line libraries, in which expression was desired), Minus (libraries from other normal adult tissues, in which expression was not desirable), and Other (libraries from fetal tissue, infant tissue, tissues found only in women, non-prostate tumors and cell lines other than prostate cell lines, in which expression was considered to be irrelevant). A summary of these library groups is presented in Table II.

Table II

Prostate cDNA Libraries and ESTs

Library	# of Libraries	# of ESTs
Plus	25	43,482
Normal	11	18,875
Tumor	11	21,769
Cell lines	3	2,838
Minus	166	
Other	287	

Each supercluster was analyzed in terms of the ESTs within the supercluster. The tissue source of each EST clone was noted and used to classify the superclusters into four groups: Type 1- EST clones found in the Plus group libraries only; no expression detected in Minus or Other group libraries; Type 2- EST clones derived from the Plus and Other group libraries only; no expression detected in the Minus group; Type 3- EST clones derived from the Plus, Minus and Other group libraries, but the number of ESTs derived from the Plus group is higher than in either the Minus or Other groups; and Type 4- EST clones derived from Plus, Minus and Other group libraries, but the number derived from the Plus group is higher than the number derived from the Minus group. This analysis identified 4,345 breast clusters (*see* Table III). From these clusters, 3,172 EST clones were ordered from Research Genetics, Inc., and were received as frozen glycerol stocks in 96-well plates.

Table III

Prostate Cluster Summary

Type	# of Superclusters	# of ESTs Ordered
1	688	677
2	2899	2484
3	85	11
4	673	0
Total	4345	3172

The EST clone inserts were PCR-amplified using amino-linked PCR primers for Synteni microarray analysis. When more than one PCR product was obtained for a particular clone, that PCR product was not used for expression analysis. In total, 2,528 clones from the electronic subtraction method were analyzed by microarray analysis to identify electronic subtraction breast clones that had high levels of tumor vs. normal

tissue mRNA. Such screens were performed using a Synteni (Palo Alto, CA) microarray, according to the manufacturer's instructions (and essentially as described by Schena et al., *Proc. Natl. Acad. Sci. USA* 93:10614-10619, 1996 and Heller et al., *Proc. Natl. Acad. Sci. USA* 94:2150-2155, 1997). Within these analyses, the clones were arrayed on the chip, which was then probed with fluorescent probes generated from normal and tumor prostate cDNA, as well as various other normal tissues. The slides were scanned and the fluorescence intensity was measured.

Clones with an expression ratio greater than 3 (*i.e.*, the level in prostate tumor and normal prostate mRNA was at least three times the level in other normal tissue mRNA) were identified as prostate tumor-specific sequences (Table IV). The sequences of these clones are provided in SEQ ID NO: 401-453, with certain novel sequences shown in SEQ ID NO: 407, 413, 416-419, 422, 426, 427 and 450.

Table IV

Prostate-tumor Specific Clones

SEQ ID NO.	Sequence Designation	Comments
401	22545	previously identified P1000C
402	22547	previously identified P704P
403	22548	known
404	22550	known
405	22551	PSA
406	22552	prostate secretory protein 94
407	22553	novel
408	22558	previously identified P509S
409	22562	glandular kallikrein
410	22565	previously identified P1000C
411	22567	PAP
412	22568	B1006C (breast tumor antigen)
413	22570	novel
414	22571	PSA
415	22572	previously identified P706P
416	22573	novel
417	22574	novel

418	22575	novel
419	22580	novel
420	22581	PAP
421	22582	prostatic secretory protein 94
422	22583	novel
423	22584	prostatic secretory protein 94
424	22585	prostatic secretory protein 94
425	22586	known
426	22587	novel
427	22588	novel
428	22589	PAP
429	22590	known
430	22591	PSA
431	22592	known
432	22593	Previously identified P777P
433	22594	T cell receptor gamma chain
434	22595	Previously identified P705P
435	22596	Previously identified P707P
436	22847	PAP
437	22848	known
438	22849	prostatic secretory protein 57
439	22851	PAP
440	22852	PAP
441	22853	PAP
442	22854	previously identified P509S
443	22855	previously identified P705P
444	22856	previously identified P774P
445	22857	PSA
446	23601	previously identified P777P
447	23602	PSA
448	23605	PSA
449	23606	PSA
450	23612	novel
451	23614	PSA
452	23618	previously identified P1000C
453	23622	previously identified P705P

Further studies on the clone of SEQ ID NO: 407 (also referred to as P1020C) led to the isolation of an extended cDNA sequence provided in SEQ ID NO: 591. This extended cDNA sequence was found to contain an open reading frame that encodes

the predicted amino acid sequence of SEQ ID NO: 592. The P1020C cDNA and amino acid sequences were found to show some similarity to the human endogenous retroviral HERV-K pol gene and protein.

5

EXAMPLE 15

FURTHER IDENTIFICATION OF PROSTATE-SPECIFIC ANTIGENS BY MICROARRAY ANALYSIS

This Example describes the isolation of additional prostate-specific polypeptides from a prostate tumor cDNA library.

10

A human prostate tumor cDNA expression library as described above was screened using microarray analysis to identify clones that display at least a three fold over-expression in prostate tumor and/or normal prostate tissue, as compared to non-prostate normal tissues (not including testis). 142 clones were identified and sequenced. Certain of these clones are shown in SEQ ID NO: 454-467. Of these sequences, SEQ ID NO: 459-
15 461 represent novel genes. The others (SEQ ID NO: 454-458 and 461-467) correspond to known sequences.

EXAMPLE 16

FURTHER CHARACTERIZATION OF PROSTATE-SPECIFIC ANTIGEN P710P

20

This Example describes the full length cloning of P710P.

The prostate cDNA library described above was screened with the P710P fragment described above. One million colonies were plated on LB/Ampicillin plates. Nylon membrane filters were used to lift these colonies, and the cDNAs picked up by these
25 filters were then denatured and cross-linked to the filters by UV light. The P710P fragment was radiolabeled and used to hybridize with the filters. Positive cDNA clones were selected and their cDNAs recovered and sequenced by an automatic Perkin Elmer/Applied Biosystems Division Sequencer. Four sequences were obtained, and are presented in SEQ ID NO: 468-471. These sequences appear to represent different splice variants of the

P710P gene. Subsequent comparison of the cDNA sequences of P710P with those in Genbank revealed homology to the DD3 gene (Genbank accession numbers AF103907 & AF103908). The cDNA sequence of DD3 is provided in SEQ ID NO: 690.

5

EXAMPLE 17

PROTEIN EXPRESSION OF PROSTATE-SPECIFIC ANTIGENS

This example describes the expression and purification of prostate-specific antigens in *E. coli*, baculovirus and mammalian cells.

10 **A) EXPRESSION OF P501S IN *E. COLI***

Expression of the full-length form of P501S was attempted by first cloning P501S without the leader sequence (amino acids 36-553 of SEQ ID NO: 113) downstream of the first 30 amino acids of the *M. tuberculosis* antigen Ra12 (SEQ ID NO: 484) in pET17b. Specifically, P501S DNA was used to perform PCR using the primers AW025 (SEQ ID NO: 485) and AW003 (SEQ ID NO: 486). AW025 is a sense cloning primer that
15 contains a HindIII site. AW003 is an antisense cloning primer that contains an EcoRI site. DNA amplification was performed using 5 µl 10X Pfu buffer, 1 µl 20 mM dNTPs, 1 µl each of the PCR primers at 10 µM concentration, 40 µl water, 1 µl Pfu DNA polymerase (Stratagene, La Jolla, CA) and 1 µl DNA at 100 ng/µl. Denaturation at 95°C was
20 performed for 30 sec, followed by 10 cycles of 95°C for 30 sec, 60°C for 1 min and by 72°C for 3 min. 20 cycles of 95°C for 30 sec, 65°C for 1 min and by 72°C for 3 min, and lastly by 1 cycle of 72°C for 10 min. The PCR product was cloned to Ra12m/pET17b using HindIII and EcoRI. The sequence of the resulting fusion construct (referred to as Ra12-P501S-F) was confirmed by DNA sequencing.

25 The fusion construct was transformed into BL21(DE3)pLysE, pLysS and CodonPlus *E. coli* (Stratagene) and grown overnight in LB broth with kanamycin. The resulting culture was induced with IPTG. Protein was transferred to PVDF membrane and blocked with 5% non-fat milk (in PBS-Tween buffer), washed three times and incubated

with mouse anti-His tag antibody (Clontech) for 1 hour. The membrane was washed 3 times and probed with HRP-Protein A (Zymed) for 30 min. Finally, the membrane was washed 3 times and developed with ECL (Amersham). No expression was detected by Western blot. Similarly, no expression was detected by Western blot when the Ra12-P501S-F fusion was used for expression in BL21CodonPlus by CE6 phage (Invitrogen).

An N-terminal fragment of P501S (amino acids 36-325 of SEQ ID NO: 113) was cloned down-stream of the first 30 amino acids of the *M. tuberculosis* antigen Ra12 in pET17b as follows. P501S DNA was used to perform PCR using the primers AW025 (SEQ ID NO: 485) and AW027 (SEQ ID NO: 487). AW027 is an antisense cloning primer that contains an EcoRI site and a stop codon. DNA amplification was performed essentially as described above. The resulting PCR product was cloned to Ra12 in pET17b at the HindIII and EcoRI sites. The fusion construct (referred to as Ra12-P501S-N) was confirmed by DNA sequencing.

The Ra12-P501S-N fusion construct was used for expression in BL21(DE3)pLysE, pLysS and CodonPlus, essentially as described above. Using Western blot analysis, protein bands were observed at the expected molecular weight of 36 kDa. Some high molecular weight bands were also observed, probably due to aggregation of the recombinant protein. No expression was detected by Western blot when the Ra12-P501S-F fusion was used for expression in BL21CodonPlus by CE6 phage.

A fusion construct comprising a C-terminal portion of P501S (amino acids 257-553 of SEQ ID NO: 113) located down-stream of the first 30 amino acids of the *M. tuberculosis* antigen Ra12 (SEQ ID NO: 484) was prepared as follows. P501S DNA was used to perform PCR using the primers AW026 (SEQ ID NO: 488) and AW003 (SEQ ID NO: 486). AW026 is a sense cloning primer that contains a HindIII site. DNA amplification was performed essentially as described above. The resulting PCR product was cloned to Ra12 in pET17b at the HindIII and EcoRI sites. The sequence for the fusion construct (referred to as Ra12-P501S-C) was confirmed.

The Ra12-P501S-C fusion construct was used for expression in BL21(DE3)pLysE, pLysS and CodonPlus, as described above. A small amount of protein

was detected by Western blot, with some molecular weight aggregates also being observed. Expression was also detected by Western blot when the Ra12-P501S-C fusion was used for expression in BL21CodonPlus induced by CE6 phage.

A fusion construct comprising a fragment of P501S (amino acids 36-298 of SEQ ID NO: 113) located down-stream of the *M. tuberculosis* antigen Ra12 (SEQ ID NO: 848) was prepared as follows. P501S DNA was used to perform PCR using the primers AW042 (SEQ ID NO: 849) and AW053 (SEQ ID NO: 850). AW042 is a sense cloning primer that contains a EcoRI site. AW053 is an antisense primer with stop and Xho I sites. DNA amplification was performed essentially as described above. The resulting PCR product was cloned to Ra12 in pET17b at the EcoRI and Xho I sites. The resulting fusion construct (referred to as Ra12-P501S-E2) was expressed in B834 (DE3) pLys S *E. coli* host cells in TB media for 2 h at room temperature. Expressed protein was purified by washing the inclusion bodies and running on a Ni-NTA column. The purified protein stayed soluble in buffer containing 20 mM Tris-HCl (pH 8), 100 mM NaCl, 10 mM β -Me and 5% glycerol. The determined cDNA and amino acid sequences for the expressed fusion protein are provided in SEQ ID NO: 851 and 852, respectfully.

B) EXPRESSION OF P501S IN BACULOVIRUS

The Bac-to-Bac baculovirus expression system (BRL Life Technologies, Inc.) was used to express P501S protein in insect cells. Full-length P501S (SEQ ID NO: 113) was amplified by PCR and cloned into the XbaI site of the donor plasmid pFastBacI. The recombinant bacmid and baculovirus were prepared according to the manufacturer's instructions. The recombinant baculovirus was amplified in Sf9 cells and the high titer viral stocks were utilized to infect High Five cells (Invitrogen) to make the recombinant protein. The identity of the full-length protein was confirmed by N-terminal sequencing of the recombinant protein and by Western blot analysis (Figure 7). Specifically, 0.6 million High Five cells in 6-well plates were infected with either the unrelated control virus BV/ECD_PD (lane 2), with recombinant baculovirus for P501S at different amounts or

MOIs (lanes 4-8), or were uninfected (lane 3). Cell lysates were run on SDS-PAGE under reducing conditions and analyzed by Western blot with the anti-P501S monoclonal antibody P501S-10E3-G4D3 (prepared as described below). Lane 1 is the biotinylated protein molecular weight marker (BioLabs).

5 The localization of recombinant P501S in the insect cells was investigated as follows. The insect cells overexpressing P501S were fractionated into fractions of nucleus, mitochondria, membrane and cytosol. Equal amounts of protein from each fraction were analyzed by Western blot with a monoclonal antibody against P501S. Due to the scheme of fractionation, both nucleus and mitochondria fractions contain some plasma
10 membrane components. However, the membrane fraction is basically free from mitochondria and nucleus. P501S was found to be present in all fractions that contain the membrane component, suggesting that P501S may be associated with plasma membrane of the insect cells expressing the recombinant protein.

C) EXPRESSION OF P501S IN MAMMALIAN CELLS

15 Full-length P501S (553AA) was cloned into various mammalian expression vectors, including pCEP4 (Invitrogen), pVR1012 (Vical, San Diego, CA) and a modified form of the retroviral vector pBMN, referred to as pBIB. Transfection of P501S/pCEP4 and P501S/pVR1012 into HEK293 fibroblasts was carried out using the Fugene transfection reagent (Boehringer Mannheim). Briefly, 2 ul of Fugene reagent was diluted
20 into 100 ul of serum-free media and incubated at room temperature for 5-10 min. This mixture was added to 1 ug of P501S plasmid DNA, mixed briefly and incubated for 30 minutes at room temperature. The Fugene/DNA mixture was added to cells and incubated for 24-48 hours. Expression of recombinant P501S in transfected HEK293 fibroblasts was detected by means of Western blot employing a monoclonal antibody to P501S.

25 Transfection of p501S/pCEP4 into CHO-K cells (American Type Culture Collection, Rockville, MD) was carried out using GenePorter transfection reagent (Gene Therapy Systems, San Diego, CA). Briefly, 15 µl of GenePorter was diluted in 500 µl of serum-free media and incubated at room temperature for 10 min. The GenePorter/media

mixture was added to 2 µg of plasmid DNA that was diluted in 500 µl of serum-free media, mixed briefly and incubated for 30 min at room temperature. CHO-K cells were rinsed in PBS to remove serum proteins, and the GenePorter/DNA mix was added and incubated for 5 hours. The transfected cells were then fed an equal volume of 2x media and incubated for 24-48 hours.

FACS analysis of P501S transiently infected CHO-K cells, demonstrated surface expression of P501S. Expression was detected using rabbit polyclonal antisera raised against a P501S peptide, as described below. Flow cytometric analysis was performed using a FaCScan (Becton Dickinson), and the data were analyzed using the Cell Quest program.

D) EXPRESSION OF P703P IN BACULOVIRUS

The cDNA for full-length P703P-DE5 (SEQ ID NO: 326), together with several flanking restriction sites, was obtained by digesting the plasmid pCDNA703 with restriction endonucleases Xba I and Hind III. The resulting restriction fragment (approx. 800 base pairs) was ligated into the transfer plasmid pFastBacI which was digested with the same restriction enzymes. The sequence of the insert was confirmed by DNA sequencing. The recombinant transfer plasmid pFBP703 was used to make recombinant bacmid DNA and baculovirus using the Bac-To-Bac Baculovirus expression system (BRL Life Technologies). High Five cells were infected with the recombinant virus BVP703, as described above, to obtain recombinant P703P protein.

E) EXPRESSION OF P788P IN *E. COLI*

A truncated, N-terminal portion, of P788P (residues 1-644 of SEQ ID NO: 777; referred to as P788P-N) fused with a C-terminal 6xHis Tag was expressed in *E. coli* as follows. P788P cDNA was amplified using the primers AW080 and AW081 (SEQ ID NO: 815 and 816). AW080 is a sense cloning primer with an NdeI site. AW081 is an antisense cloning primer with a XhoI site. The PCR-amplified P788P, as well as the vector pCRX1, were digested with NdeI and XhoI. Vector and insert were ligated and transformed into

NovaBlue cells. Colonies were randomly screened for insert and then sequenced. P788P-N clone #6 was confirmed to be identical to the designed construct. The expression construct P788P-N #6/pCRX1 was transformed into *E. coli* BL21 CodonPlus-RIL competent cells. After induction, most of the cells grew well, achieving OD₆₀₀ of greater than 2.0 after 3 hr. Coomassie stained SDS-PAGE showed an over-expressed band at about 75 kD. Western blot analysis using a 6xHisTag antibody confirmed the band was P788P-N. The determined cDNA sequence for P788P-N is provided in SEQ ID NO: 817, with the corresponding amino acid sequence being provided in SEQ ID NO: 818.

F) EXPRESSION OF P510S IN *E. COLI*

The P510S protein has 9 potential transmembrane domains and is predicted to be located at the plasma membrane. The C-terminal protein of this protein, as well as the predicted third extracellular domain of P510S were expressed in *E. coli* as follows.

The expression construct referred to as Ra12-P501S-C was designed to have a 6 HisTag at the N-terminal end, followed by the *M. tuberculosis* antigen Ra12 (SEQ ID NO: 819) and then the C-terminal portion of P510S (amino residues 1176-1261 of SEQ ID NO: 538). Full-length P510S was used to amplify the P510S-C fragment by PCR using the primers AW056 and AW057 (SEQ ID NO: 820 and 821, respectively). AW056 is a sense cloning primer with an EcoRI site. AW057 is an antisense primer with stop and XhoI sites. The amplified P501S fragment and Ra12/pCRX1 were digested with EcoRI and XhoI and then purified. The insert and vector were ligated together and transformed into NovaBlue. Colonies were randomly screened for insert and sequences. For protein expression, the expression construct was transformed into *E. coli* BL21 (DE3) CodonPlus-RIL competent cells. A mini-induction screen was performed to optimize the expression conditions. After induction the cells grew well, achieving OD₆₀₀ nm greater than 2.0 after 3 hours. Coomassie stain SDS-PAGE showed a highly over-expressed band at approx. 30 kD. Though this is higher than the expected molecular weight, western blot analysis was positive, showing this band to be the His tag-containing protein. The optimized culture conditions are as follows. Dilute overnight culture/daytime culture (LB + kanamycin +

chloramphenicol) into 2xYT (with kanamycin and chloramphenicol) at a ratio of 25 ml culture to 1 liter 2xYT. Allow to grow at 37 °C until OD600 = 0.6. Take an aliquot out as T0 sample. Add 1 mM IPTG and allow to grow at 30 °C for 3 hours. Take out a T3 sample, spin down cells and store at -80 °C. The determined cDNA and amino acid
 5 sequences for the Ra12-P510S-C construct are provided in SEQ ID NO: 822 and 825, respectively.

The expression construct P510S-C was designed to have a 5' added start codon and a glycine (GGA) codon and then the P510S C terminal fragment followed by the in frame 6x histidine tag and stop codon from the pET28b vector. The cloning strategy is similar to
 10 that used for Ra12-P510S-C, except that the PCR primers employed were those shown in SEQ ID NO: 828 and 829, respectively and the NcoI/XhoI cut in pET28b was used. The primer of SEQ ID NO: 828 created a 5' NcoI site and added a start codon. The antisense primer of SEQ ID NO: 829 creates a XhoI site on P510S C terminal fragment. Clones were confirmed by sequencing. For protein expression, the expression construct was
 15 transformed into *E. coli* BL21 (DE3) CodonPlus-RIL competent cells. An OD600 of greater than 2.0 was obtained 30 hours after induction. Coomassie stained SDS-PAGE showed an over-expressed band at about 11 kD. Western blot analysis confirmed that the band was P510S-C, as did N-terminal protein sequencing. The optimized culture conditions are as follows: dilute overnight culture/daytime culture (LB + kanamycin +
 20 chloramphenicol) into 2x YT (+ kanamycin and chloramphenicol) at a ratio of 25 mL culture to 1 liter 2x YT, and allow to grow at 37 °C until an OD 600 of about 0.5 is reached. Take out an aliquot as T0 sample. Add 1 mM IPTG and allow to grow at 30 °C for 3 hours. Spin down the cells and store at -80 °C until purification. The determined cDNA and amino acid sequence for the P510S-C construct are shown in SEQ ID NO: 823
 25 and 826, respectively.

The predicted third extracellular domain of P510S (P510S-E3; residues 328-676 of SEQ ID NO: 538) was expressed in *E. coli* as follows. The P510S fragment was amplified by PCR using the primers shown in SEQ ID NO: 830 and 831. The primer of SEQ ID NO: 830 is a sense primer with an NdeI site for use in ligating into pPDM. The

primer of SEQ ID NO: 831 is an antisense primer with an added XhoI site for use in ligating into pPDM. The resulting fragment was cloned to pPDM at the NdeI and XhoI sites. Clones were confirmed by sequencing. For protein expression, the clone was transformed into *E. coli* BL21 (DE3) CodonPlus-RIL competent cells. After induction, an OD600 of greater than 2.0 was achieved after 3 hours. Coomassie stained SDS-PAGE showed an over-expressed band at about 39 kD, and N-terminal sequencing confirmed the N-terminal to be that of P510S-E3. Optimized culture conditions are as follows: dilute overnight culture/daytime culture (LB + kanamycin + chloramphenicol) into 2x YT (kanamycin and chloramphenicol) at a ratio of 25 ml culture to 1 liter 2x YT. Allow to grow at 37 °C until OD 600 equals 0.6. Take out an aliquot as T0 sample. Add 1 mM IPTG and allow to grow at 30 °C for 3 hours. Take out a T3 sample, spin down the cells and store at -80 °C until purification. The determined cDNA and amino acid sequences for the P501S-E3 construct are provided in SEQ ID NO: 824 and 827, respectively.

G) EXPRESSION OF P775S IN *E. COLI*

The antigen P775P contains multiple open reading frames (ORF). The third ORF, encoding the protein of SEQ ID NO: 483, has the best motif score. An expression fusion construct containing the *M. tuberculosis* antigen Ra12 (SEQ ID NO: 819) and P775P-ORF3 with an N-terminal 6x HisTag was prepared as follows. P775P-ORF3 was amplified using the sense PCR primers of SEQ ID NO: 832 and the anti-sense PCR primer of SEQ ID NO: 833. The PCR amplified fragment of P775P and Ra12/pCRX1 were digested with the restriction enzymes EcoRI and XhoI. Vector and insert were ligated and then transformed into NovaBlue cells. Colonies were randomly screened for insert and then sequenced. A clone having the desired sequence was transformed into *E. coli* BL21 (DE3) CodonPlus-RIL competent cells. Two hours after induction, the cell density peaked at OD600 of approximately 1.8. Coomassie stained SDS-PAGE showed an over-expressed band at about 31 kD. Western blot using 6x HisTag antibody confirmed that the band was Ra12-P775P-ORF3. The determined cDNA and amino acid sequences for the fusion construct are provided in SEQ ID NO: 834 and 835, respectively.

H) EXPRESSION OF A P703P HIS TAG FUSION PROTEIN IN E. COLI

The cDNA for the coding region of P703P was prepared by PCR using the primers of SEQ ID NO: 836 and 837. The PCR product was digested with EcoRI restriction enzyme, gel purified and cloned into a modified pET28 vector with a His tag in frame, which had been digested with Eco72I and EcoRI restriction enzymes. The correct construct was confirmed by DNA sequence analysis and then transformed into *E. coli* BL21 (DE3) pLys S expression host cells. The determined amino acid and cDNA sequences for the expressed recombinant P703P are provided in SEQ ID NO: 838 and 839, respectively.

I) EXPRESSION OF A P705P HIS TAG FUSION PROTEIN IN E. COLI

The cDNA for the coding region of P705P was prepared by PCR using the primers of SEQ ID NO: 840 and 841. The PCR product was digested with EcoRI restriction enzyme, gel purified and cloned into a modified pET28 vector with a His tag in frame, which had been digested with Eco72I and EcoRI restriction enzymes. The correct construct was confirmed by DNA sequence analysis and then transformed into *E. coli* BL21 (DE3) pLys S and BL21 (DE3) CodonPlus expression host cells. The determined amino acid and cDNA sequences for the expressed recombinant P705P are provided in SEQ ID NO: 842 and 843, respectively.

J) EXPRESSION OF A P711P HIS TAG FUSION PROTEIN IN E. COLI

The cDNA for the coding region of P711P was prepared by PCR using the primers of SEQ ID NO: 844 and 845. The PCR product was digested with EcoRI restriction enzyme, gel purified and cloned into a modified pET28 vector with a His tag in frame, which had been digested with Eco72I and EcoRI restriction enzymes. The correct construct was confirmed by DNA sequence analysis and then transformed into *E. coli* BL21 (DE3) pLys S and BL21 (DE3) CodonPlus expression host cells. The determined amino acid and cDNA sequences for the expressed recombinant P711P are provided in SEQ ID NO: 846 and 847, respectively.

EXAMPLE 18

**PREPARATION AND CHARACTERIZATION OF ANTIBODIES
AGAINST PROSTATE-SPECIFIC POLYPEPTIDES**

**A) PREPARATION AND CHARACTERIZATION OF POLYCLONAL ANTIBODIES AGAINST
P703P, P504S AND P509S**

Polyclonal antibodies against P703P, P504S and P509S were prepared as follows.

Each prostate tumor antigen expressed in an *E. coli* recombinant expression system was grown overnight in LB broth with the appropriate antibiotics at 37°C in a shaking incubator. The next morning, 10 ml of the overnight culture was added to 500 ml to 2x YT plus appropriate antibiotics in a 2L-baffled Erlenmeyer flask. When the Optical Density (at 560 nm) of the culture reached 0.4-0.6, the cells were induced with IPTG (1 mM). Four hours after induction with IPTG, the cells were harvested by centrifugation. The cells were then washed with phosphate buffered saline and centrifuged again. The supernatant was discarded and the cells were either frozen for future use or immediately processed. Twenty ml of lysis buffer was added to the cell pellets and vortexed. To break

open the *E. coli* cells, this mixture was then run through the French Press at a pressure of 16,000 psi. The cells were then centrifuged again and the supernatant and pellet were checked by SDS-PAGE for the partitioning of the recombinant protein. For proteins that localized to the cell pellet, the pellet was resuspended in 10 mM Tris pH 8.0, 1% CHAPS and the inclusion body pellet was washed and centrifuged again. This procedure was repeated twice more. The washed inclusion body pellet was solubilized with either 8 M urea or 6 M guanidine HCl containing 10 mM Tris pH 8.0 plus 10 mM imidazole. The solubilized protein was added to 5 ml of nickel-chelate resin (Qiagen) and incubated for 45 min to 1 hour at room temperature with continuous agitation. After incubation, the resin and protein mixture were poured through a disposable column and the flow through was collected. The column was then washed with 10-20 column volumes of the solubilization buffer. The antigen was then eluted from the column using 8M urea, 10 mM Tris pH 8.0 and 300 mM imidazole and collected in 3 ml fractions. A SDS-PAGE gel was run to determine which fractions to pool for further purification.

As a final purification step, a strong anion exchange resin such as HiPrepQ (Biorad) was equilibrated with the appropriate buffer and the pooled fractions from above were loaded onto the column. Each antigen was eluted off the column with a increasing salt gradient. Fractions were collected as the column was run and another SDS-PAGE gel was run to determine which fractions from the column to pool. The pooled fractions were dialyzed against 10 mM Tris pH 8.0. The proteins were then vialled after filtration through a 0.22 micron filter and the antigens were frozen until needed for immunization.

Four hundred micrograms of each prostate antigen was combined with 100 micrograms of muramyl dipeptide (MDP). Every four weeks rabbits were boosted with 100 micrograms mixed with an equal volume of Incomplete Freund's Adjuvant (IFA). Seven days following each boost, the animal was bled. Sera was generated by incubating the blood at 4°C for 12-4 hours followed by centrifugation.

Ninety-six well plates were coated with antigen by incubating with 50 microliters (typically 1 microgram) of recombinant protein at 4 °C for 20 hours. 250 microliters of BSA blocking buffer was added to the wells and incubated at room

temperature for 2 hours. Plates were washed 6 times with PBS/0.01% Tween. Rabbit sera was diluted in PBS. Fifty microliters of diluted sera was added to each well and incubated at room temperature for 30 min. Plates were washed as described above before 50 microliters of goat anti-rabbit horse radish peroxidase (HRP) at a 1:10000 dilution was added and incubated at room temperature for 30 min. Plates were again washed as described above and 100 microliters of TMB microwell peroxidase substrate was added to each well. Following a 15 min incubation in the dark at room temperature, the colorimetric reaction was stopped with 100 microliters of 1N H₂SO₄ and read immediately at 450 nm. All polyclonal antibodies showed immunoreactivity to the appropriate antigen.

10 **B) PREPARATION AND CHARACTERIZATION OF ANTIBODIES AGAINST P501S**

A murine monoclonal antibody directed against the carboxy-terminus of the prostate-specific antigen P501S was prepared as follows.

A truncated fragment of P501S (amino acids 355-526 of SEQ ID NO: 113) was generated and cloned into the pET28b vector (Novagen) and expressed in *E. coli* as a thioredoxin fusion protein with a histidine tag. The trx-P501S fusion protein was purified by nickel chromatography, digested with thrombin to remove the trx fragment and further purified by an acid precipitation procedure followed by reverse phase HPLC.

Mice were immunized with truncated P501S protein. Serum bleeds from mice that potentially contained anti-P501S polyclonal sera were tested for P501S-specific reactivity using ELISA assays with purified P501S and trx-P501S proteins. Serum bleeds that appeared to react specifically with P501S were then screened for P501S reactivity by Western analysis. Mice that contained a P501S-specific antibody component were sacrificed and spleen cells were used to generate anti-P501S antibody producing hybridomas using standard techniques. Hybridoma supernatants were tested for P501S-specific reactivity initially by ELISA, and subsequently by FACS analysis of reactivity with P501S transduced cells. Based on these results, a monoclonal hybridoma referred to as 10E3 was chosen for further subcloning. A number of subclones were generated, tested for specific reactivity to P501S using ELISA and typed for IgG isotype. The results of this

analysis are shown below in Table V. Of the 16 subclones tested, the monoclonal antibody 10E3-G4-D3 was selected for further study.

Table V

5 Isotype analysis of murine anti-P501S monoclonal antibodies

Hybridoma clone	Isotype	Estimated [Ig] in supernatant (μg/ml)
4D11	IgG1	14.6
1G1	IgG1	0.6
4F6	IgG1	72
4H5	IgG1	13.8
4H5-E12	IgG1	10.7
4H5-EH2	IgG1	9.2
4H5-H2-A10	IgG1	10
4H5-H2-A3	IgG1	12.8
4H5-H2-A10-G6	IgG1	13.6
4H5-H2-B11	IgG1	12.3
10E3	IgG2a	3.4
10E3-D4	IgG2a	3.8
10E3-D4-G3	IgG2a	9.5
10E3-D4-G6	IgG2a	10.4
10E3-E7	IgG2a	6.5
8H12	IgG2a	0.6

The specificity of 10E3-G4-D3 for P501S was examined by FACS analysis. Specifically, cells were fixed (2% formaldehyde, 10 minutes), permeabilized (0.1% saponin, 10 minutes) and stained with 10E3-G4-D3 at 0.5 – 1 μg/ml, followed by incubation with a secondary, FITC-conjugated goat anti-mouse Ig antibody (Pharmingen, San Diego, CA). Cells were then analyzed for FITC fluorescence using an Excalibur fluorescence activated cell sorter. For FACS analysis of transduced cells, B-LCL were retrovirally transduced with P501S. For analysis of infected cells, B-LCL were infected with a vaccinia vector that expresses P501S. To demonstrate specificity in these assays, B-LCL transduced with a different antigen (P703P) and uninfected B-LCL vectors were utilized. 10E3-G4-D3 was shown to bind with P501S-transduced B-LCL and also with P501S-infected B-LCL, but not with either uninfected cells or P703P-transduced cells.

To determine whether the epitope recognized by 10E3-G4-D3 was found on the surface or in an intracellular compartment of cells, B-LCL were transduced with P501S or HLA-B8 as a control antigen and either fixed and permeabilized as described above or directly stained with 10E3-G4-D3 and analyzed as above. Specific recognition of P501S
 5 by 10E3-G4-D3 was found to require permeabilization, suggesting that the epitope recognized by this antibody is intracellular.

The reactivity of 10E3-G4-D3 with the three prostate tumor cell lines Lncap, PC-3 and DU-145, which are known to express high, medium and very low levels of P501S, respectively, was examined by permeabilizing the cells and treating them as
 10 described above. Higher reactivity of 10E3-G4-D3 was seen with Lncap than with PC-3, which in turn showed higher reactivity than DU-145. These results are in agreement with the real time PCR and demonstrate that the antibody specifically recognizes P501S in these tumor cell lines and that the epitope recognized in prostate tumor cell lines is also intracellular.

Specificity of 10E3-G4-D3 for P501S was also demonstrated by Western blot analysis. Lysates from the prostate tumor cell lines Lncap, DU-145 and PC-3, from P501S-transiently transfected HEK293 cells, and from non-transfected HEK293 cells were generated. Western blot analysis of these lysates with 10E3-G4-D3 revealed a 46 kDa immunoreactive band in Lncap, PC-3 and P501S-transfected HEK cells, but not in DU-145
 15 cells or non-transfected HEK293 cells. P501S mRNA expression is consistent with these results since semi-quantitative PCR analysis revealed that P501S mRNA is expressed in Lncap, to a lesser but detectable level in PC-3 and not at all in DU-145 cells. Bacterially expressed and purified recombinant P501S (referred to as P501SStr2) was recognized by 10E3-G4-D3 (24 kDa), as was full-length P501S that was transiently expressed in HEK293
 20 cells using either the expression vector VR1012 or pCEP4. Although the predicted molecular weight of P501S is 60.5 kDa, both transfected and “native” P501S run at a slightly lower mobility due to its hydrophobic nature.

Immunohistochemical analysis was performed on prostate tumor and a panel of normal tissue sections (prostate, adrenal, breast, cervix, colon, duodenum, gall

bladder, ileum, kidney, ovary, pancreas, parotid gland, skeletal muscle, spleen and testis). Tissue samples were fixed in formalin solution for 24 hours and embedded in paraffin before being sliced into 10 micron sections. Tissue sections were permeabilized and incubated with 10E3-G4-D3 antibody for 1 hr. HRP-labeled anti-mouse followed by
 5 incubation with DAB chromogen was used to visualize P501S immunoreactivity. P501S was found to be highly expressed in both normal prostate and prostate tumor tissue but was not detected in any of the other tissues tested.

To identify the epitope recognized by 10E3-G4-D3, an epitope mapping approach was pursued. A series of 13 overlapping 20-21 mers (5 amino acid overlap; SEQ
 10 ID NO: 489-501) was synthesized that spanned the fragment of P501S used to generate 10E3-G4-D3. Flat bottom 96 well microtiter plates were coated with either the peptides or the P501S fragment used to immunize mice, at 1 microgram/ml for 2 hours at 37 °C. Wells were then aspirated and blocked with phosphate buffered saline containing 1% (w/v) BSA for 2 hours at room temperature, and subsequently washed in PBS containing 0.1% Tween
 15 20 (PBST). Purified antibody 10E3-G4-D3 was added at 2 fold dilutions (1000 ng – 16 ng) in PBST and incubated for 30 minutes at room temperature. This was followed by washing 6 times with PBST and subsequently incubating with HRP-conjugated donkey anti-mouse IgG (H+L)Affinipure F(ab') fragment (Jackson ImmunoResearch, West Grove, PA) at 1:20000 for 30 minutes. Plates were then washed and incubated for 15 minutes in
 20 tetramethyl benzidine. Reactions were stopped by the addition of 1N sulfuric acid and plates were read at 450 nm using an ELISA plate reader. As shown in Fig. 8, reactivity was seen with the peptide of SEQ ID NO: 496 (corresponding to amino acids 439-459 of P501S) and with the P501S fragment but not with the remaining peptides, demonstrating that the epitope recognized by 10E3-G4-D3 is localized to amino acids 439-459 of SEQ ID
 25 NO: 113.

In order to further evaluate the tissue specificity of P501S, multi-array immunohistochemical analysis was performed on approximately 4700 different human tissues encompassing all the major normal organs as well as neoplasias derived from these tissues. Sixty-five of these human tissue samples were of prostate origin. Tissue sections

0.6 mm in diameter were formalin-fixed and paraffin embedded. Samples were pretreated with HIER using 10 mM citrate buffer pH 6.0 and boiling for 10 min. Sections were stained with 10E3-G4-D3 and P501S immunoreactivity was visualized with HRP. All the 65 prostate tissues samples (5 normal, 55 untreated prostate tumors, 5 hormone refractory prostate tumors) were positive, showing distinct perinuclear staining. All other tissues examined were negative for P501S expression.

C) PREPARATION AND CHARACTERIZATION OF ANTIBODIES AGAINST P503S

A fragment of P503S (amino acids 113-241 of SEQ ID NO: 114) was expressed and purified from bacteria essentially as described above for P501S and used to immunize both rabbits and mice. Mouse monoclonal antibodies were isolated using standard hybridoma technology as described above. Rabbit monoclonal antibodies were isolated using Selected Lymphocyte Antibody Method (SLAM) technology at Immgenics Pharmaceuticals (Vancouver, BC, Canada). Table VI, below, lists the monoclonal antibodies that were developed against P503S.

Table VI

Antibody	Species
20D4	Rabbit
JA1	Rabbit
1A4	Mouse
1C3	Mouse
1C9	Mouse
1D12	Mouse
2A11	Mouse
2H9	Mouse
4H7	Mouse
8A8	Mouse
8D10	Mouse
9C12	Mouse
6D12	Mouse

The DNA sequences encoding the complementarity determining regions (CDRs) for the rabbit monoclonal antibodies 20D4 and JA1 were determined and are provided in SEQ ID NO: 502 and 503, respectively.

In order to better define the epitope binding region of each of the antibodies, a series of overlapping peptides were generated that span amino acids 109-213 of SEQ ID NO: 114. These peptides were used to epitope map the anti-P503S monoclonal antibodies by ELISA as follows. The recombinant fragment of P503S that was employed as the immunogen was used as a positive control. Ninety-six well microtiter plates were coated with either peptide or recombinant antigen at 20 ng/well overnight at 4 °C. Plates were aspirated and blocked with phosphate buffered saline containing 1% (w/v) BSA for 2 hours at room temperature then washed in PBS containing 0.1% Tween 20 (PBST). Purified rabbit monoclonal antibodies diluted in PBST were added to the wells and incubated for 30 min at room temperature. This was followed by washing 6 times with PBST and incubation with Protein-A HRP conjugate at a 1:2000 dilution for a further 30 min. Plates were washed six times in PBST and incubated with tetramethylbenzidine (TMB) substrate for a further 15 min. The reaction was stopped by the addition of 1N sulfuric acid and plates were read at 450 nm using at ELISA plate reader. ELISA with the mouse monoclonal antibodies was performed with supernatants from tissue culture run neat in the assay.

All of the antibodies bound to the recombinant P503S fragment, with the exception of the negative control SP2 supernatant. 20D4, JA1 and 1D12 bound strictly to peptide #2101 (SEQ ID NO: 504), which corresponds to amino acids 151-169 of SEQ ID NO: 114. 1C3 bound to peptide #2102 (SEQ ID NO: 505), which corresponds to amino acids 165-184 of SEQ ID NO: 114. 9C12 bound to peptide #2099 (SEQ ID NO: 522), which corresponds to amino acids 120-139 of SEQ ID NO: 114. The other antibodies bind to regions that were not examined in these studies.

Subsequent to epitope mapping, the antibodies were tested by FACS analysis on a cell line that stably expressed P503S to confirm that the antibodies bind to cell surface epitopes. Cells stably transfected with a control plasmid were employed as a

negative control. Cells were stained live with no fixative. 0.5 ug of anti-P503S monoclonal antibody was added and cells were incubated on ice for 30 min before being washed twice and incubated with a FITC-labelled goat anti-rabbit or mouse secondary antibody for 20 min. After being washed twice, cells were analyzed with an Excalibur
 5 fluorescent activated cell sorter. The monoclonal antibodies 1C3, 1D12, 9C12, 20D4 and JA1, but not 8D3, were found to bind to a cell surface epitope of P503S.

In order to determine which tissues express P503S, immunohistochemical analysis was performed, essentially as described above, on a panel of normal tissues (prostate, adrenal, breast, cervix, colon, duodenum, gall bladder, ileum, kidney, ovary,
 10 pancreas, parotid gland, skeletal muscle, spleen and testis). HRP-labeled anti-mouse or anti-rabbit antibody followed by incubation with TMB was used to visualize P503S immunoreactivity. P503S was found to be highly expressed in prostate tissue, with lower levels of expression being observed in cervix, colon, ileum and kidney, and no expression being observed in adrenal, breast, duodenum, gall bladder, ovary, pancreas, parotid gland,
 15 skeletal muscle, spleen and testis.

Western blot analysis was used to characterize anti-P503S monoclonal antibody specificity. SDS-PAGE was performed on recombinant (rec) P503S expressed in and purified from bacteria and on lysates from HEK293 cells transfected with full length P503S. Protein was transferred to nitrocellulose and then Western blotted with each of the
 20 anti-P503S monoclonal antibodies (20D4, JA1, 1D12, 6D12 and 9C12) at an antibody concentration of 1 ug/ml. Protein was detected using horse radish peroxidase (HRP) conjugated to either a goat anti-mouse monoclonal antibody or to protein A-sepharose. The monoclonal antibody 20D4 detected the appropriate molecular weight 14 kDa recombinant P503S (amino acids 113-241) and the 23.5 kDa species in the HEK293 cell
 25 lysates transfected with full length P503S. Other anti-P503S monoclonal antibodies displayed similar specificity by Western blot.

D) PREPARATION AND CHARACTERIZATION OF ANTIBODIES AGAINST P703P

Rabbits were immunized with either a truncated (P703Ptr1; SEQ ID NO: 172) or full-length mature form (P703Pfl; SEQ ID NO: 523) of recombinant P703P protein was expressed in and purified from bacteria as described above. Affinity purified polyclonal antibody was generated using immunogen P703Pfl or P703Ptr1 attached to a solid support. Rabbit monoclonal antibodies were isolated using SLAM technology at Immgenics Pharmaceuticals. Table VII below lists both the polyclonal and monoclonal antibodies that were generated against P703P.

Table VII

Antibody	Immunogen	Species/type
Aff. Purif. P703P (truncated); #2594	P703Ptr1	Rabbit polyclonal
Aff. Purif. P703P (full length); #9245	P703Pfl	Rabbit polyclonal
2D4	P703Ptr1	Rabbit monoclonal
8H2	P703Ptr1	Rabbit monoclonal
7H8	P703Ptr1	Rabbit monoclonal

The DNA sequences encoding the complementarity determining regions (CDRs) for the rabbit monoclonal antibodies 8H2, 7H8 and 2D4 were determined and are provided in SEQ ID NO: 506-508, respectively.

Epitope mapping studies were performed as described above. Monoclonal antibodies 2D4 and 7H8 were found to specifically bind to the peptides of SEQ ID NO: 509 (corresponding to amino acids 145-159 of SEQ ID NO: 172) and SEQ ID NO: 510 (corresponding to amino acids 11-25 of SEQ ID NO: 172), respectively. The polyclonal antibody 2594 was found to bind to the peptides of SEQ ID NO: 511-514, with the polyclonal antibody 9427 binding to the peptides of SEQ ID NO: 515-517.

The specificity of the anti-P703P antibodies was determined by Western blot analysis as follows. SDS-PAGE was performed on (1) bacterially expressed recombinant antigen; (2) lysates of HEK293 cells and Ltk^{-/-} cells either untransfected or transfected with a plasmid expressing full length P703P; and (3) supernatant isolated from

these cell cultures. Protein was transferred to nitrocellulose and then Western blotted using the anti-P703P polyclonal antibody #2594 at an antibody concentration of 1 ug/ml. Protein was detected using horse radish peroxidase (HRP) conjugated to an anti-rabbit antibody. A 35 kDa immunoreactive band could be observed with recombinant P703P. Recombinant

5 P703P runs at a slightly higher molecular weight since it is epitope tagged. In lysates and supernatants from cells transfected with full length P703P, a 30 kDa band corresponding to P703P was observed. To assure specificity, lysates from HEK293 cells stably transfected with a control plasmid were also tested and were negative for P703P expression. Other anti-P703P antibodies showed similar results.

10 Immunohistochemical studies were performed as described above, using anti-P703P monoclonal antibody. P703P was found to be expressed at high levels in normal prostate and prostate tumor tissue but was not detectable in all other tissues tested (breast tumor, lung tumor and normal kidney).

15

EXAMPLE 19

CHARACTERIZATION OF CELL SURFACE EXPRESSION AND CHROMOSOME LOCALIZATION OF THE PROSTATE-SPECIFIC ANTIGEN P501S

20 This example describes studies demonstrating that the prostate-specific antigen P501S is expressed on the surface of cells, together with studies to determine the probable chromosomal location of P501S.

The protein P501S (SEQ ID NO: 113) is predicted to have 11 transmembrane domains. Based on the discovery that the epitope recognized by the anti-P501S monoclonal antibody 10E3-G4-D3 (described above in Example 17) is intracellular,

25 it was predicted that following transmembrane determinants would allow the prediction of extracellular domains of P501S. Fig. 9 is a schematic representation of the P501S protein showing the predicted location of the transmembrane domains and the intracellular epitope described in Example 17. Underlined sequence represents the predicted transmembrane domains, bold sequence represents the predicted extracellular domains, and italicized

sequence represents the predicted intracellular domains. Sequence that is both bold and underlined represents sequence employed to generate polyclonal rabbit serum. The location of the transmembrane domains was predicted using HHMTOP as described by Tusnady and Simon (Principles Governing Amino Acid Composition of Integral

5 Membrane Proteins: Applications to Topology Prediction, *J. Mol. Biol.* 283:489-506, 1998).

Based on Fig. 9, the P501S domain flanked by the transmembrane domains corresponding to amino acids 274-295 and 323-342 is predicted to be extracellular. The peptide of SEQ ID NO: 518 corresponds to amino acids 306-320 of P501S and lies in the

10 predicted extracellular domain. The peptide of SEQ ID NO: 519, which is identical to the peptide of SEQ ID NO: 518 with the exception of the substitution of the histidine with an asparagine, was synthesized as described above. A Cys-Gly was added to the C-terminus of the peptide to facilitate conjugation to the carrier protein. Cleavage of the peptide from the solid support was carried out using the following cleavage mixture: trifluoroacetic

15 acid:ethanediol:thioanisole:water:phenol (40:1:2:2:3). After cleaving for two hours, the peptide was precipitated in cold ether. The peptide pellet was then dissolved in 10% v/v acetic acid and lyophilized prior to purification by C18 reverse phase hplc. A gradient of 5-60% acetonitrile (containing 0.05% TFA) in water (containing 0.05% TFA) was used to elute the peptide. The purity of the peptide was verified by hplc and mass spectrometry,

20 and was determined to be >95%. The purified peptide was used to generate rabbit polyclonal antisera as described above.

Surface expression of P501S was examined by FACS analysis. Cells were stained with the polyclonal anti-P501S peptide serum at 10 µg/ml, washed, incubated with a secondary FITC-conjugated goat anti-rabbit Ig antibody (ICN), washed and analyzed for

25 FITC fluorescence using an Excalibur fluorescence activated cell sorter. For FACS analysis of transduced cells, B-LCL were retrovirally transduced with P501S. To demonstrate specificity in these assays, B-LCL transduced with an irrelevant antigen (P703P) or nontransduced were stained in parallel. For FACS analysis of prostate tumor cell lines, Lncap, PC-3 and DU-145 were utilized. Prostate tumor cell lines were

dissociated from tissue culture plates using cell dissociation medium and stained as above. All samples were treated with propidium iodide (PI) prior to FACS analysis, and data was obtained from PI-excluding (*i.e.*, intact and non-permeabilized) cells. The rabbit polyclonal serum generated against the peptide of SEQ ID NO: 519 was shown to
 5 specifically recognize the surface of cells transduced to express P501S, demonstrating that the epitope recognized by the polyclonal serum is extracellular.

To determine biochemically if P501S is expressed on the cell surface, peripheral membranes from Lncap cells were isolated and subjected to Western blot analysis. Specifically, Lncap cells were lysed using a dounce homogenizer in 5 ml of
 10 homogenization buffer (250 mM sucrose, 10 mM HEPES, 1mM EDTA, pH 8.0, 1 complete protease inhibitor tablet (Boehringer Mannheim)). Lysate samples were spun at 1000 g for 5 min at 4 °C. The supernatant was then spun at 8000g for 10 min at 4 °C. Supernatant from the 8000g spin was recovered and subjected to a 100,000g spin for 30 min at 4 °C to recover peripheral membrane. Samples were then separated by SDS-PAGE
 15 and Western blotted with the mouse monoclonal antibody 10E3-G4-D3 (described above in Example 17) using conditions described above. Recombinant purified P501S, as well as HEK293 cells transfected with and over-expressing P501S were included as positive controls for P501S detection. LCL cell lysate was included as a negative control. P501S could be detected in Lncap total cell lysate, the 8000g (internal membrane) fraction and
 20 also in the 100,000g (plasma membrane) fraction. These results indicate that P501S is expressed at, and localizes to, the peripheral membrane.

To demonstrate that the rabbit polyclonal antiserum generated to the peptide of SEQ ID NO: 519 specifically recognizes this peptide as well as the corresponding native peptide of SEQ ID NO: 518, ELISA analyses were performed. For these analyses, flat-
 25 bottomed 96 well microtiter plates were coated with either the peptide of SEQ ID NO: 519, the longer peptide of SEQ ID NO: 520 that spans the entire predicted extracellular domain, the peptide of SEQ ID NO: 521 which represents the epitope recognized by the P501S-specific antibody 10E3-G4-D3, or a P501S fragment (corresponding to amino acids 355-526 of SEQ ID NO: 113) that does not include the immunizing peptide sequence, at 1

µg/ml for 2 hours at 37 °C. Wells were aspirated, blocked with phosphate buffered saline containing 1% (w/v) BSA for 2 hours at room temperature and subsequently washed in PBS containing 0.1% Tween 20 (PBST). Purified anti-P501S polyclonal rabbit serum was added at 2 fold dilutions (1000 ng - 125 ng) in PBST and incubated for 30 min at room temperature. This was followed by washing 6 times with PBST and incubating with HRP-conjugated goat anti-rabbit IgG (H+L) Affinipure F(ab') fragment at 1:20000 for 30 min. Plates were then washed and incubated for 15 min in tetramethyl benzidine. Reactions were stopped by the addition of 1N sulfuric acid and plates were read at 450 nm using an ELISA plate reader. As shown in Fig. 11, the anti-P501S polyclonal rabbit serum specifically recognized the peptide of SEQ ID NO: 519 used in the immunization as well as the longer peptide of SEQ ID NO: 520, but did not recognize the irrelevant P501S-derived peptides and fragments.

In further studies, rabbits were immunized with peptides derived from the P501S sequence and predicted to be either extracellular or intracellular, as shown in Fig. 9. Polyclonal rabbit sera were isolated and polyclonal antibodies in the serum were purified, as described above. To determine specific reactivity with P501S, FACS analysis was employed, utilizing either B-LCL transduced with P501S or the irrelevant antigen P703P, of B-LCL infected with vaccinia virus-expressing P501S. For surface expression, dead and non-intact cells were excluded from the analysis as described above. For intracellular staining, cells were fixed and permeabilized as described above. Rabbit polyclonal serum generated against the peptide of SEQ ID NO: 548, which corresponds to amino acids 181-198 of P501S, was found to recognize a surface epitope of P501S. Rabbit polyclonal serum generated against the peptide SEQ ID NO: 551, which corresponds to amino acids 543-553 of P501S, was found to recognize an epitope that was either potentially extracellular or intracellular since in different experiments intact or permeabilized cells were recognized by the polyclonal sera. Based on similar deductive reasoning, the sequences of SEQ ID NO: 541-547, 549 and 550, which correspond to amino acids 109-122, 539-553, 509-520, 37-54, 342-359, 295-323, 217-274, 143-160 and 75-88,

respectively, of P501S, can be considered to be potential surface epitopes of P501S recognized by antibodies.

The chromosomal location of P501S was determined using the GeneBridge 4 Radiation Hybrid panel (Research Genetics). The PCR primers of SEQ ID NO: 528 and 529 were employed in PCR with DNA pools from the hybrid panel according to the manufacturer's directions. After 38 cycles of amplification, the reaction products were separated on a 1.2% agarose gel, and the results were analyzed through the Whitehead Institute/MIT Center for Genome Research web server (<http://www-genome.wi.mit.edu/cgi-bin/contig/rhmapper.pl>) to determine the probable chromosomal location. Using this approach, P501S was mapped to the long arm of chromosome 1 at WI-9641 between q32 and q42. This region of chromosome 1 has been linked to prostate cancer susceptibility in hereditary prostate cancer (Smith *et al. Science* 274:1371-1374, 1996 and Berthon *et al. Am. J. Hum. Genet.* 62:1416-1424, 1998). These results suggest that P501S may play a role in prostate cancer malignancy.

EXAMPLE 20

REGULATION OF EXPRESSION OF THE PROSTATE-SPECIFIC ANTIGEN P501S

Steroid (androgen) hormone modulation is a common treatment modality in prostate cancer. The expression of a number of prostate tissue-specific antigens have previously been demonstrated to respond to androgen. The responsiveness of the prostate-specific antigen P501S to androgen treatment was examined in a tissue culture system as follows.

Cells from the prostate tumor cell line LNCaP were plated at 1.5×10^6 cells/T75 flask (for RNA isolation) or 3×10^5 cells/well of a 6-well plate (for FACS analysis) and grown overnight in RPMI 1640 media containing 10% charcoal-stripped fetal calf serum (BRL Life Technologies, Gaithersburg, MD). Cell culture was continued for an additional 72 hours in RPMI 1640 media containing 10% charcoal-stripped fetal calf serum, with 1 nM of the synthetic androgen Methyltrienolone (R1881; New England

Nuclear) added at various time points. Cells were then harvested for RNA isolation and FACS analysis at 0, 1, 2, 4, 8, 16, 24, 28 and 72-hours post androgen addition. FACS analysis was performed using the anti-P501S antibody 10E3-G4-D3 and permeabilized cells.

5 For Northern analysis, 5-10 micrograms of total RNA was run on a formaldehyde denaturing gel, transferred to Hybond-N nylon membrane (Amersham Pharmacia Biotech, Piscataway, NJ), cross-linked and stained with methylene blue. The filter was then prehybridized with Church's Buffer (250 mM Na_2HPO_4 , 70 mM H_3PO_4 , 1 mM EDTA, 1% SDS, 1% BSA in pH 7.2) at 65 °C for 1 hour. P501S DNA was labeled
10 with ^{32}P using High Prime random-primed DNA labeling kit (Boehringer Mannheim). Unincorporated label was removed using MicroSpin S300-HR columns (Amersham Pharmacia Biotech). The RNA filter was then hybridized with fresh Church's Buffer containing labeled cDNA overnight, washed with 1X SCP (0.1 M NaCl, 0.03 M $\text{Na}_2\text{HPO}_4 \cdot 7\text{H}_2\text{O}$, 0.001 M Na_2EDTA), 1% sarkosyl (n-lauroylsarcosine) and exposed to X-
15 ray film.

Using both FACS and Northern analysis, P501S message and protein levels were found in increase in response to androgen treatment.

EXAMPLE 20

20 PREPARATION OF FUSION PROTEINS OF PROSTATE-SPECIFIC ANTIGENS

The example describes the preparation of a fusion protein of the prostate-specific antigen P703P and a truncated form of the known prostate antigen PSA. The truncated form of PSA has a 21 amino acid deletion around the active serine site. The
25 expression construct for the fusion protein also has a restriction site at 3' end, immediately prior to the termination codon, to aid in adding cDNA for additional antigens.

The full-length cDNA for PSA was obtained by RT-PCR from a pool of RNA from human prostate tumor tissues using the primers of SEQ ID NO: 607 and 608, and cloned in the vector pCR-Blunt II-TOPO. The resulting cDNA was employed as a

template to make two different fragments of PSA by PCR with two sets of primers (SEQ ID NO: 609 and 610; and SEQ ID NO: 611 and 612). The PCR products having the expected size were used as templates to make truncated forms of PSA by PCR with the primers of SEQ ID NO: 611 and 613, which generated PSA (delta 208-218 in amino acids).

- 5 The cDNA for the mature form of P703P with a 6X histidine tag at the 5' end, was prepared by PCR with P703P and the primers of SEQ ID NO: 614 and 615. The cDNA for the fusion of P703P with the truncated form of PSA (referred to as FOPP) was then obtained by PCR using the modified P703P cDNA and the truncated form of PSA cDNA as templates and the primers of SEQ ID NO: 614 and 615. The FOPP cDNA was cloned
- 10 into the NdeI site and XhoI site of the expression vector pCRX1, and confirmed by DNA sequencing. The determined cDNA sequence for the fusion construct FOPP is provided in SEQ ID NO: 616, with the amino acid sequence being provided in SEQ ID NO: 617.

- The fusion FOPP was expressed as a single recombinant protein in *E. coli* as follows. The expression plasmid pCRX1FOPP was transformed into the *E. coli* strain BL21-CodonPlus
- 15 RIL. The transformant was shown to express FOPP protein upon induction with 1 mM IPTG. The culture of the corresponding expression clone was inoculated into 25 ml LB broth containing 50 ug/ml kanamycin and 34 ug/ml chloramphenicol, grown at 37 °C to OD600 of about 1, and stored at 4 °C overnight. The culture was diluted into 1 liter of TB LB containing 50 ug/ml kanamycin and 34 ug/ml chloramphenicol, and grown at 37 °C to
 - 20 OD600 of 0.4. IPTG was added to a final concentration of 1 mM, and the culture was incubated at 30 °C for 3 hours. The cells were pelleted by centrifugation at 5,000 RPM for 8 min. To purify the protein, the cell pellet was suspended in 25 ml of 10 mM Tris-Cl pH 8.0, 2mM PMSF, complete protease inhibitor and 15 ug lysozyme. The cells were lysed at 4 °C for 30 minutes, sonicated several times and the lysate centrifuged for 30 minutes at
 - 25 10,000 x g. The precipitate, which contained the inclusion body, was washed twice with 10 mM Tris-Cl pH 8.0 and 1% CHAPS. The inclusion body was dissolved in 40 ml of 10 mM Tris-Cl pH 8.0, 100 mM sodium phosphate and 8 M urea. The solution was bound to 8 ml Ni-NTA (Qiagen) for one hour at room temperature. The mixture was poured into a 25 ml column and washed with 50 ml of 10 mM Tris-Cl pH 6.3, 100 mM sodium

phosphate, 0.5% DOC and 8M urea. The bound protein was eluted with 350 mM imidazole, 10 mM Tris-Cl pH 8.0, 100 mM sodium phosphate and 8 M urea. The fractions containing FOPP proteins were combined and dialyzed extensively against 10 mM Tris-Cl pH 4.6, aliquoted and stored at - 70 °C.

5

EXAMPLE 21

REAL-TIME PCR CHARACTERIZATION OF THE PROSTATE-SPECIFIC ANTIGEN P501S IN PERIPHERAL BLOOD OF PROSTATE CANCER PATIENTS

- 10 Circulating epithelial cells were isolated from fresh blood of normal individuals and metastatic prostate cancer patients, mRNA isolated and cDNA prepared using real-time PCR procedures. Real-time PCR was performed with the TaqmanTM procedure using both gene specific primers and probes to determine the levels of gene expression.
- 15 Epithelial cells were enriched from blood samples using an immunomagnetic bead separation method (Dynal A.S., Oslo, Norway). Isolated cells were lysed and the magnetic beads removed. The lysate was then processed for poly A+ mRNA isolation using magnetic beads coated with Oligo(dT)25. After washing the beads in buffer, bead/poly A+ RNA samples were suspended in 10 mM Tris HCl pH 8.0 and
- 20 subjected to reversed transcription. The resulting cDNA was subjected to real-time PCR using gene specific primers. Beta-actin content was also determined and used for normalization. Samples with P501S copies greater than the mean of the normal samples + 3 standard deviations were considered positive. Real time PCR on blood samples was performed using the TaqmanTM procedure but extending to 50 cycles using forward and
- 25 reverse primers and probes specific for P501S. Of the eight samples tested, 6 were positive for P501S and β -actin signal. The remaining 2 samples had no detectable β -actin or P501S. No P501S signal was observed in the four normal blood samples tested.

EXAMPLE 22

EXPRESSION OF THE PROSTATE-SPECIFIC ANTIGENS P703P AND P501S IN SCID MOUSE-PASSAGED PROSTATE TUMORS

5 When considering the effectiveness of antigens in the treatment of prostate cancer, the continued presence of the antigens in tumors during androgen ablation therapy is important. The presence of the prostate-specific antigens P703P and P501S in prostate tumor samples grown in SCID mice in the presence of testosterone was evaluated as follows.

10 Two prostate tumors that had metastasized to the bone were removed from patients, implanted into SCID mice and grown in the presence of testosterone. Tumors were evaluated for mRNA expression of P703P, P501S and PSA using quantitative real time PCR with the SYBR green assay method. Expression of P703P and P501S in a prostate tumor was used as a positive control and the absence in normal intestine and
15 normal heart as negative controls. In both cases, the specific mRNA was present in late passage tumors. Since the bone metastases were grown in the presence of testosterone, this implies that the presence of these genes would not be lost during androgen ablation therapy.

20 EXAMPLE 23

ANTI-P503S MONOCLONAL ANTIBODY INHIBITS TUMOR GROWTH *IN VIVO*

 The ability of the anti-P503S monoclonal antibody 20D4 to suppress tumor formation in mice was examined as follows.

 Ten SCID mice were injected subcutaneously with HEK293 cells that
25 expressed P503S. Five mice received 150 micrograms of 20D4 intravenously at day 0 (time of tumor cell injection), day 5 and day 9. Tumor size was measured for 50 days. Of the five animals that received no 20D4, three formed detectable tumors after about 2 weeks which continued to enlarge throughout the study. In contrast, none of the five mice that

received 20D4 formed tumors. These results demonstrate that the anti-P503S Mab 20D4 displays potent anti-tumor activity *in vivo*.

From the foregoing, it will be appreciated that, although specific
5 embodiments of the invention have been described herein for the purposes of illustration, various modifications may be made without deviating from the spirit and scope of the invention. Accordingly, the present invention is not limited except as by the appended claims.

CLAIMS

What is claimed:

1. An isolated polypeptide, comprising at least an immunogenic portion of a prostate-specific protein, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(a) sequences recited in SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-361, 363-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-689, 691-698, 702-705, 709-772, 779, 817, 823 and 824;

(b) sequences that hybridize to a sequence recited in any one of SEQ ID NOs: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-361, 363-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-689, 691-698, 702-705, 709-772, 779, 817, 823 and 824 under moderately stringent conditions; and

(c) complements of sequences of (a) or (b).

2. An isolated polypeptide according to claim 1, wherein the polypeptide comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-361, 363-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434,

435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-689, 691-698, 702-705, 709-772, 779, 817, 823 and 824, or a complement of any of the foregoing polynucleotide sequences.

3. An isolated polypeptide comprising a sequence recited in any one of SEQ ID NO: 108, 112, 113, 114, 172, 176, 178, 327, 329, 331, 338, 339, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534, 537-551, 553-568, 573-586, 588-590, 592, 706-708, 778, 780, 781, 810, 811, 814, 818, 826, 827, 853, 855, 858 and 860-862.

4. An isolated polynucleotide encoding at least 15 amino acid residues of a prostate-specific protein, or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with antigen-specific antisera is not substantially diminished, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide comprising a sequence recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-361, 363-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-689, 691-698, 702-705, 709-772, 779, 817, 823 and 824, or a complement of any of the foregoing sequences.

5. An isolated polynucleotide encoding a prostate-specific protein, or a variant thereof, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide comprising a sequence recited in any one of SEQ ID NOs: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-361, 363-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-

461, 468-471, 472-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-689, 691-698, 702-705, 709-772, 779, 817, 823 and 824, or a complement of any of the foregoing sequences.

6. An isolated polynucleotide, comprising a sequence recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-361, 363-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-689, 691-698, 702-705, 709-772, 779, 817, 823 and 824.

7. An isolated polynucleotide, comprising a sequence that hybridizes to a sequence recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-361, 363-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-689, 691-698, 702-705, 709-772, 779, 817, 823 and 824 under moderately stringent conditions.

8. An isolated polynucleotide complementary to a polynucleotide according to any one of claims 4-7.

9. An expression vector, comprising a polynucleotide according to any one of claims 4-8.

10. A host cell transformed or transfected with an expression vector according to claim 9.

11. An isolated antibody, or antigen-binding fragment thereof, that specifically binds to a prostate-specific protein that comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-361, 363-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-689, 691-698, 702-705, 709-772, 779, 817, 823 and 824, or a complement of any of the foregoing polynucleotide sequences.

12. A fusion protein, comprising at least one polypeptide according to claim 1.

13. A fusion protein according to claim 12, wherein the fusion protein comprises an expression enhancer that increases expression of the fusion protein in a host cell transfected with a polynucleotide encoding the fusion protein.

14. A fusion protein according to claim 12, wherein the fusion protein comprises a T helper epitope that is not present within the polypeptide of claim 1.

15. A fusion protein according to claim 12, wherein the fusion protein comprises an affinity tag.

16. An isolated polynucleotide encoding a fusion protein according to claim 12.

17. A pharmaceutical composition, comprising a physiologically acceptable carrier and at least one component selected from the group consisting of:

(a) a polypeptide according to claim 1;

- (b) a polynucleotide according to claim 4;
- (c) an antibody according to claim 11;
- (d) a fusion protein according to claim 12; and
- (e) a polynucleotide according to claim 16.

18. An immunogenic composition comprising an immunostimulant and at least one component selected from the group consisting of:

- (a) a polypeptide according to claim 1;
- (b) a polynucleotide according to claim 4;
- (c) an antibody according to claim 11;
- (d) a fusion protein according to claim 12; and
- (e) a polynucleotide according to claim 16.

19. An immunogenic composition according to claim 18, wherein the immunostimulant is an adjuvant.

20. An immunogenic composition according to claim 18, wherein the immunostimulant induces a predominantly Type I response.

21. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a pharmaceutical composition according to claim 17.

22. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of an immunogenic composition according to claim 18.

23. A pharmaceutical composition comprising an antigen-presenting cell that expresses a polypeptide according to claim 1, in combination with a pharmaceutically acceptable carrier or excipient.

24. A pharmaceutical composition according to claim 23, wherein the antigen presenting cell is a dendritic cell or a macrophage.

✓ 25. An immunogenic composition comprising an antigen-presenting cell that expresses a polypeptide comprising at least an immunogenic portion of a prostate-specific protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(a) sequences recited in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823 and 824;

(b) sequences that hybridize to a sequence recited in any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823 and 824 under moderately stringent conditions; and

(c) complements of sequences of (i) or (ii);
in combination with an immunostimulant.

26. An immunogenic composition according to claim 25, wherein the immunostimulant is an adjuvant.

27. An immunogenic composition according to claim 25, wherein the immunostimulant induces a predominantly Type I response.

28. An immunogenic composition according to claim 25, wherein the antigen-presenting cell is a dendritic cell.

29. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of an antigen-presenting cell that expresses a polypeptide comprising at least an immunogenic portion of a prostate-specific protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(a) sequences recited in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823 and 824;

(b) sequences that hybridize to a sequence recited in any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823 and 824 under moderately stringent conditions; and

(c) complements of sequences of (i) or (ii) encoded by a polynucleotide recited in any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823 and 824;

and thereby inhibiting the development of a cancer in the patient.

30. A method according to claim 29, wherein the antigen-presenting cell is a dendritic cell.

31. A method according to any one of claims 21, 22 and 29, wherein the cancer is prostate cancer.

32. A method for removing tumor cells from a biological sample, comprising contacting a biological sample with T cells that specifically react with a prostate-specific protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(i) polynucleotides recited in any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823 and 824; and

(ii) complements of the foregoing polynucleotides;

wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the antigen from the sample.

33. A method according to claim 32, wherein the biological sample is blood or a fraction thereof.

34. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient a biological sample treated according to the method of claim 32.

35. A method for stimulating and/or expanding T cells specific for a prostate-specific protein, comprising contacting T cells with at least one component selected from the group consisting of:

(a) polypeptides comprising at least an immunogenic portion of a prostate-specific protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(i) sequences recited in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823 and 824;

(ii) sequences that hybridize to a sequence recited in any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823 and 824 under moderately stringent conditions; and

(iii) complements of sequences of (i) or (ii);

- (b) polynucleotides encoding a polypeptide of (a); and
- (c) antigen presenting cells that express a polypeptide of (a);

under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells.

36. An isolated T cell population, comprising T cells prepared according to the method of claim 35.

37. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a T cell population according to claim 36.

~~38.~~ A method for inhibiting the development of a cancer in a patient, comprising the steps of:

(a) incubating CD4⁺ and/or CD8⁺ T cells isolated from a patient with at least one component selected from the group consisting of:

(i) polypeptides comprising at least an immunogenic portion of a prostate-specific protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(1) sequences recited in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823 and 824;

(2) sequences that hybridize to a sequence recited in any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823 and 824 under moderately stringent conditions; and

(3) complements of sequences of (1) or (2);

(ii) polynucleotides encoding a polypeptide of (i); and

(iii) antigen presenting cells that expresses a polypeptide of (i);
such that T cells proliferate; and

(b) administering to the patient an effective amount of the proliferated T cells,
and thereby inhibiting the development of a cancer in the patient.

39. A method for inhibiting the development of a cancer in a patient,
comprising the steps of:

(a) incubating CD4⁺ and/or CD8⁺ T cells isolated from a patient with at least
one component selected from the group consisting of:

(i) polypeptides comprising at least an immunogenic portion of a
prostate-specific protein, or a variant thereof, wherein the tumor protein comprises an amino acid
sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(1) sequences recited in SEQ ID NO: 1-111, 115-171, 173-175,
177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530,
531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823 and
824;

(2) sequences that hybridize to a sequence recited in any one of
SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375,
381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-
705, 709-774, 777, 789, 817, 823 and 824 under moderately stringent conditions; and

(3) complements of sequences of (1) or (2);

(ii) polynucleotides encoding a polypeptide of (i); and

(iii) antigen presenting cells that express a polypeptide of (i);

such that T cells proliferate;

(b) cloning at least one proliferated cell to provide cloned T cells; and

(c) administering to the patient an effective amount of the cloned T cells, and
thereby inhibiting the development of a cancer in the patient.

40. A method for determining the presence or absence of a cancer in a patient, comprising the steps of:

- (a) contacting a biological sample obtained from a patient with a binding agent that binds to a prostate-specific protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823 and 824 or a complement of any of the foregoing polynucleotide sequences;
- (b) detecting in the sample an amount of polypeptide that binds to the binding agent; and
- (c) comparing the amount of polypeptide to a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient.

41. A method according to claim 40, wherein the binding agent is an antibody.

42. A method according to claim 43, wherein the antibody is a monoclonal antibody.

43. A method according to claim 40, wherein the cancer is prostate cancer.

44. A method for monitoring the progression of a cancer in a patient, comprising the steps of:

- (a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to a prostate-specific protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823 and 824 or a complement of any of the foregoing polynucleotide sequences;

- (b) detecting in the sample an amount of polypeptide that binds to the binding agent;
- (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and
- (d) comparing the amount of polypeptide detected in step (c) to the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

45. A method according to claim 44, wherein the binding agent is an antibody.

46. A method according to claim 45, wherein the antibody is a monoclonal antibody.

47. A method according to claim 44, wherein the cancer is a prostate cancer.

48. A method for determining the presence or absence of a cancer in a patient, comprising the steps of:

(a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate-specific protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823 and 824, or a complement of any of the foregoing polynucleotide sequences;

(b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; and

(c) comparing the amount of polynucleotide that hybridizes to the oligonucleotide to a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient.

49. A method according to claim 48, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.

50. A method according to claim 48, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.

51. A method for monitoring the progression of a cancer in a patient, comprising the steps of:

(a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate-specific protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823 and 824, or a complement of any of the foregoing polynucleotide sequences;

(b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide;

(c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and

(d) comparing the amount of polynucleotide detected in step (c) to the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

52. A method according to claim 51, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.

53. A method according to claim 51, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.

54. A diagnostic kit, comprising:

- (a) one or more antibodies according to claim 11; and
- (b) a detection reagent comprising a reporter group.

55. A kit according to claim 54, wherein the antibodies are immobilized on a solid support.

56. A kit according to claim 54, wherein the detection reagent comprises an anti-immunoglobulin, protein G, protein A or lectin.

57. A kit according to claim 54, wherein the reporter group is selected from the group consisting of radioisotopes, fluorescent groups, luminescent groups, enzymes, biotin and dye particles.

58. An oligonucleotide comprising 10 to 40 contiguous nucleotides that hybridize under moderately stringent conditions to a polynucleotide that encodes a prostate-specific protein, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-361, 363-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-689, 691-698, 702-705, 709-772, 779, 817, 823 and 824, or a complement of any of the foregoing polynucleotides.

59. A oligonucleotide according to claim 58, wherein the oligonucleotide comprises 10-40 contiguous nucleotides recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326,

328, 330, 332, 334, 350-361, 363-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-689, 691-698, 702-705, 709-772, 779, 817, 823 and 824.

60. A diagnostic kit, comprising:

(a) an oligonucleotide according to claim 59; and

(b) a diagnostic reagent for use in a polymerase chain reaction or hybridization assay.

61. A fusion protein according to claim 12, wherein the fusion protein comprises an amino acid sequence selected from the group consisting of: SEQ ID NO: 617, 825, 835 838, 842, 846 and 852.

63. A fusion protein according to claim 12, wherein the fusion protein comprises an amino acid sequence encoded by a sequence selected from the group consisting of: SEQ ID NO: 616, 822, 834, 839, 843, 847 and 851.

COMPOSITIONS AND METHODS FOR THE THERAPY
AND DIAGNOSIS OF PROSTATE CANCER

ABSTRACT OF THE DISCLOSURE

Compositions and methods for the therapy and diagnosis of cancer, such as prostate cancer, are disclosed. Compositions may comprise one or more prostate-specific proteins, immunogenic portions thereof, or polynucleotides that encode such portions. Alternatively, a therapeutic composition may comprise an antigen presenting cell that expresses a prostate-specific protein, or a T cell that is specific for cells expressing such a protein. Such compositions may be used, for example, for the prevention and treatment of diseases such as prostate cancer. Diagnostic methods based on detecting a prostate-specific protein, or mRNA encoding such a protein, in a sample are also provided.

006280" 9625960

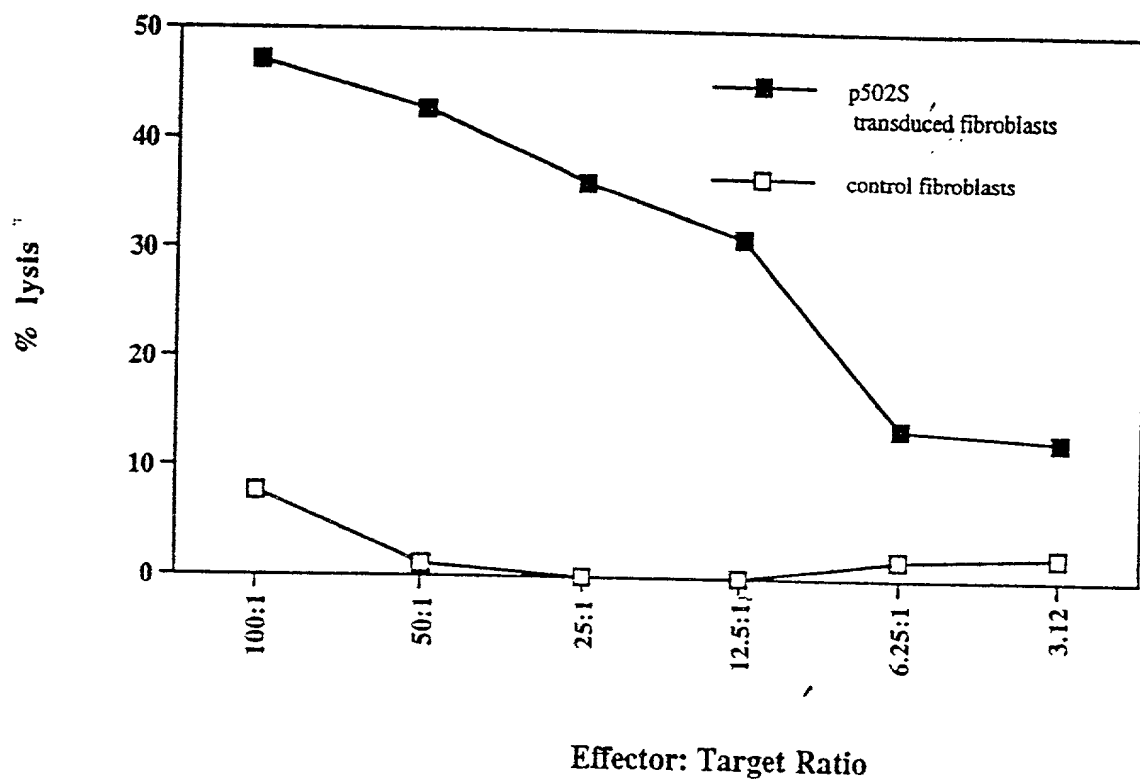


FIG. 1

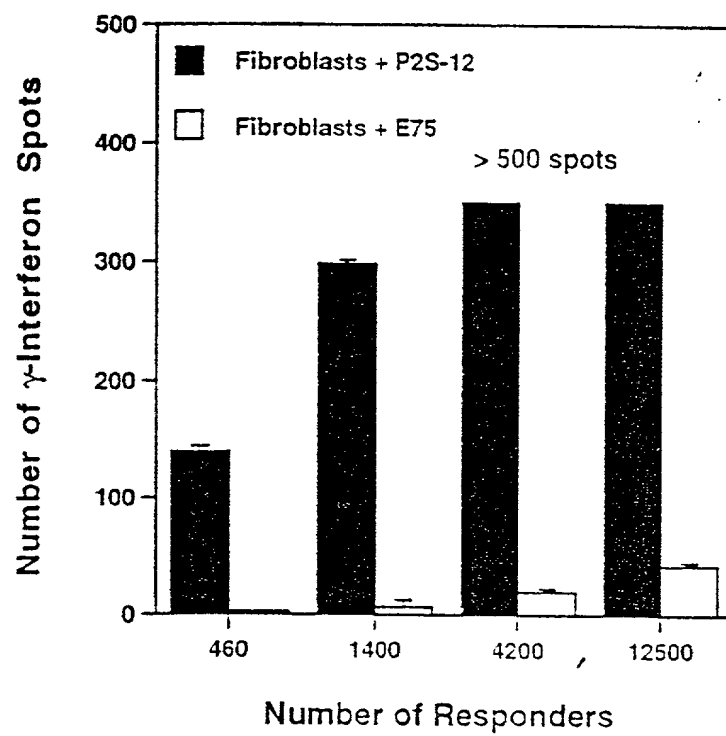


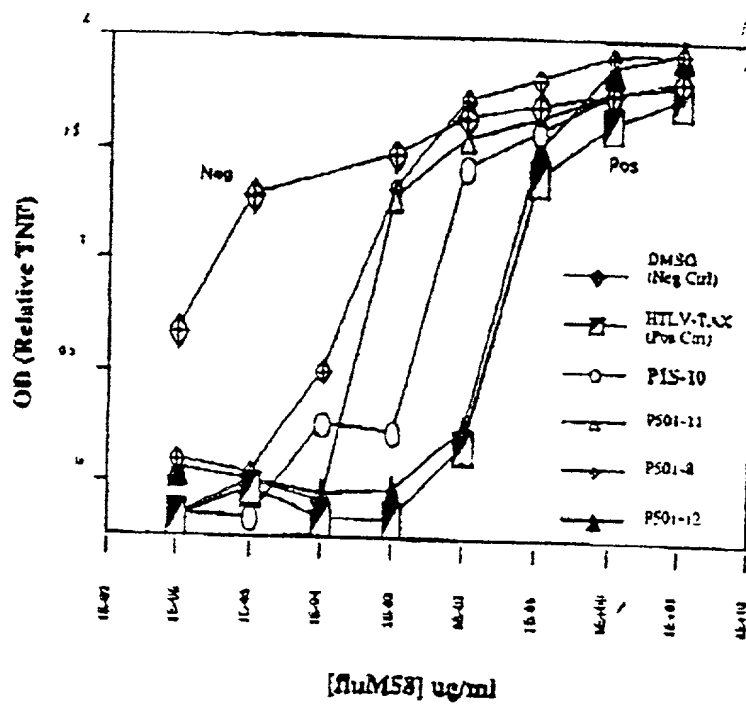
FIG. 2A

A bar chart comparing the number of γ -interferon spots for two cell lines: Fibroblasts / P502S (black bars) and Fibroblasts / HER-2 (white bars). The x-axis represents the 'Number of Responders' with categories 460, 1400, 4200, and 12500. The y-axis represents the 'Number of γ -Interferon Spots' ranging from 0 to 125. Error bars are present on all bars.

Number of Responders	Fibroblasts / P502S (Spots)	Fibroblasts / HER-2 (Spots)
460	~6	~3
1400	~16	~2
4200	~58	~12
12500	~95	~30

FIG. 2B

005280" 3627530



Figure

3

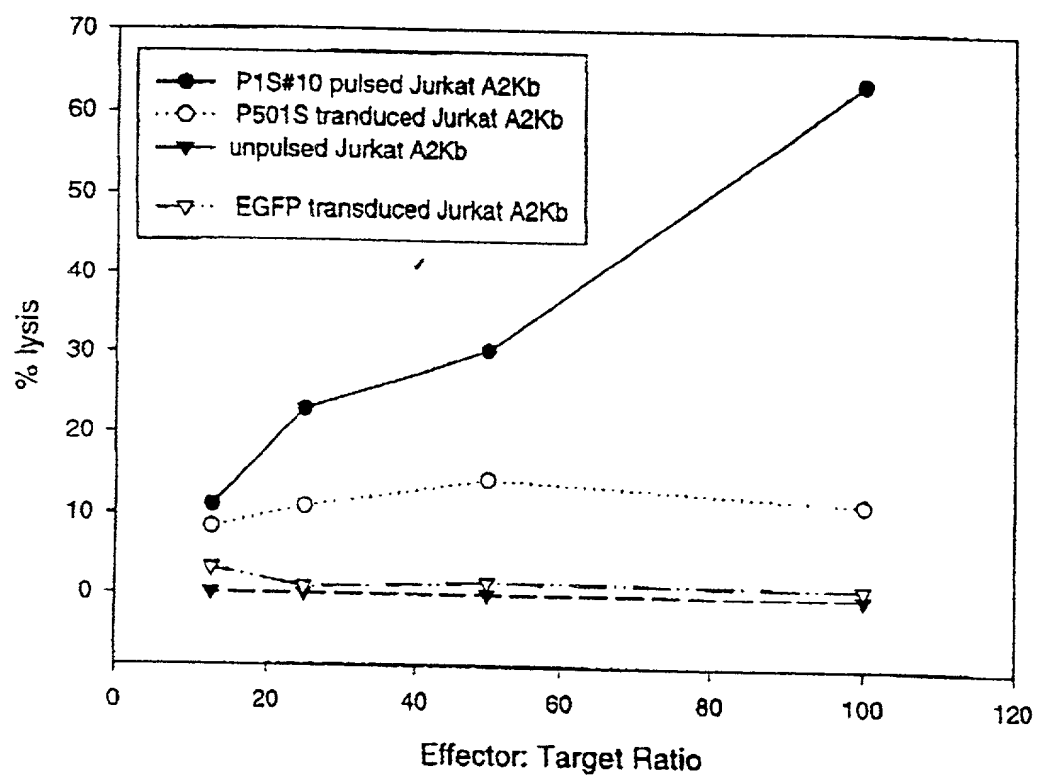


Figure 4

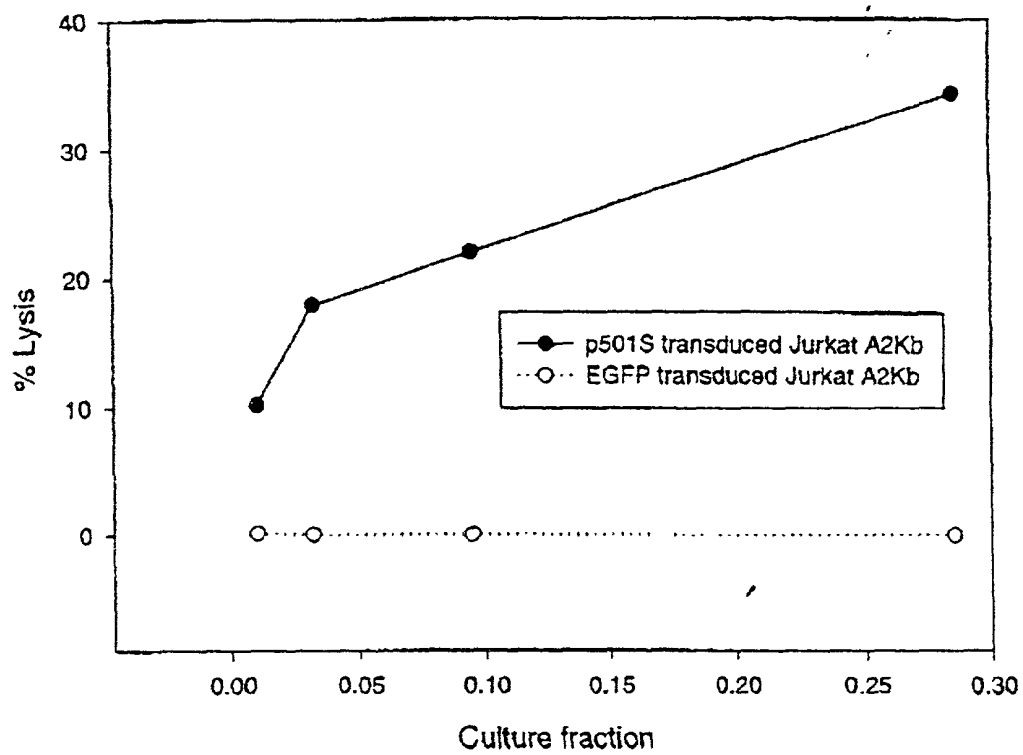


Figure 5

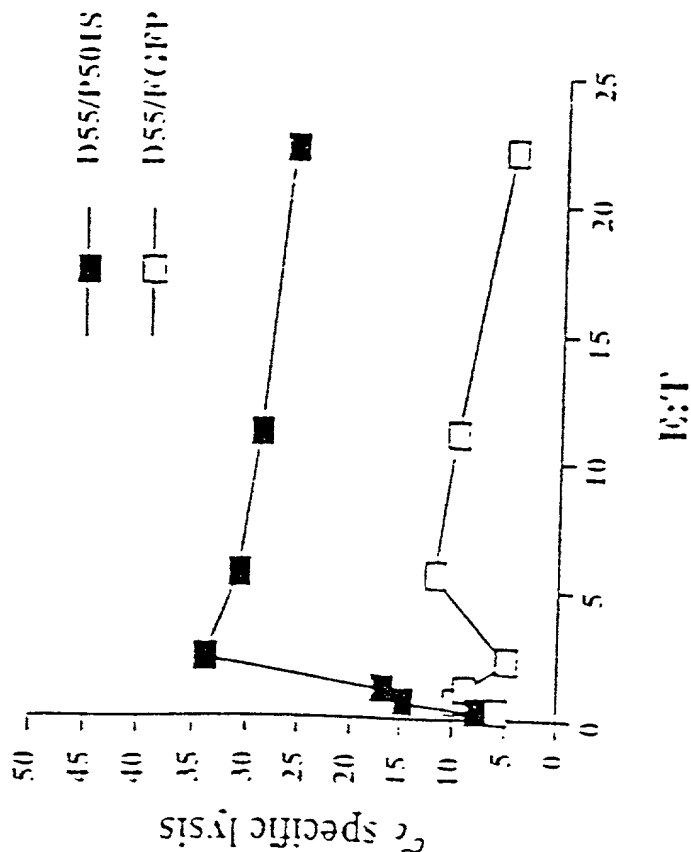


Fig. 6A

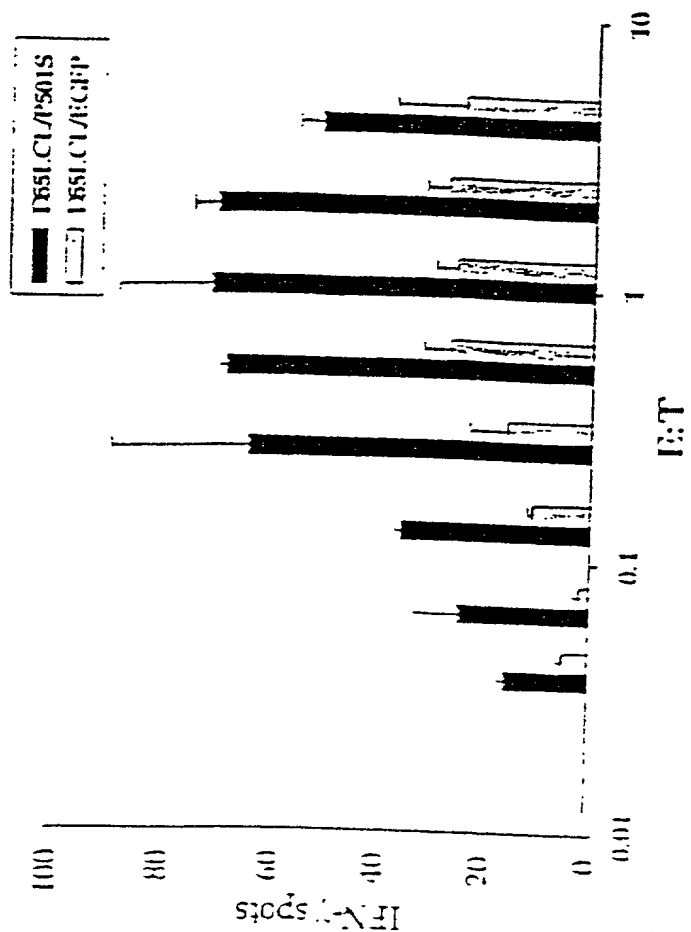
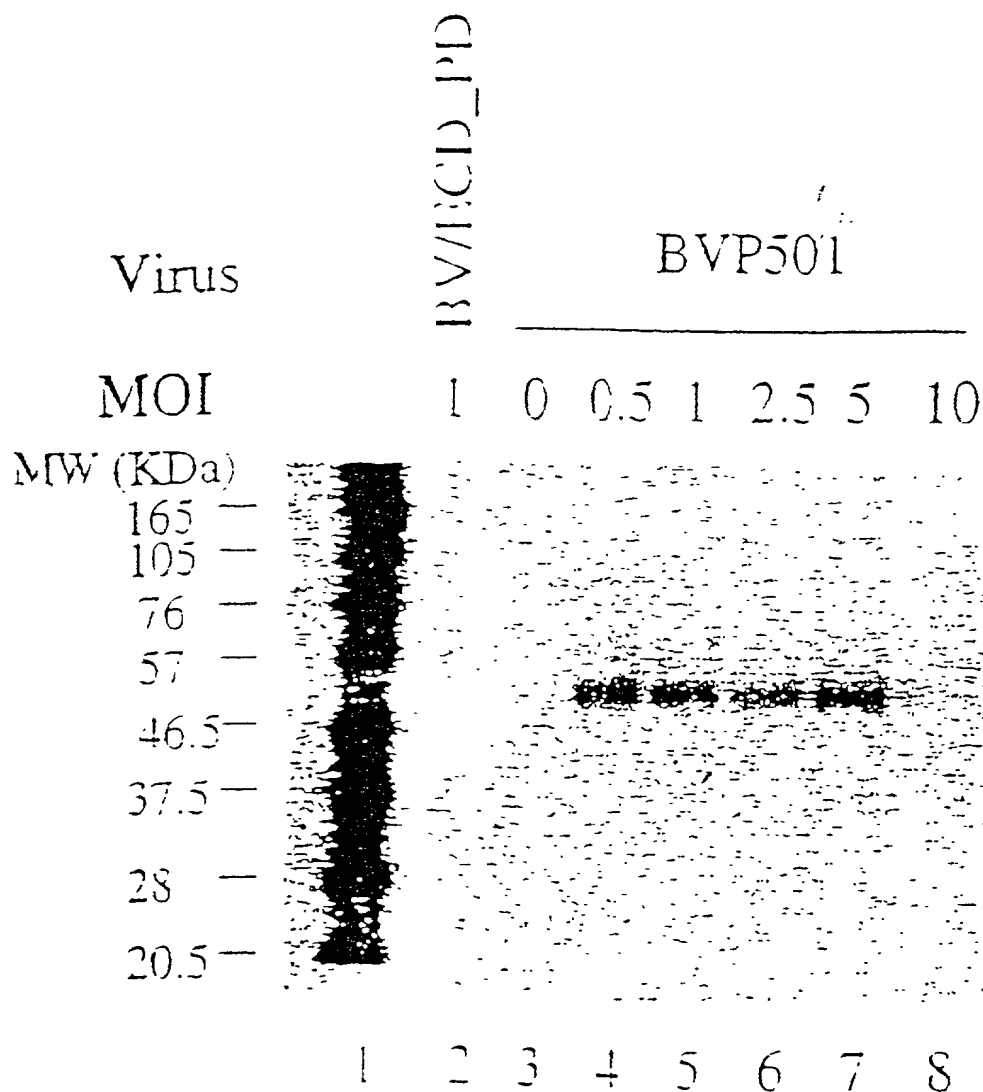


Fig. 6B

Expression of P501S by the Baculovirus Expression System



0.6 million high cells in 6-well plate were infected with an unrelated control virus BV/ECD_PD (lane 2), without virus (lane 3), or with recombinant baculovirus for P501 at different MOIs (lane 4-8). Cell lysates were run on SDS-PAGE under the reducing condition and analyzed by Western blot with a monoclonal antibody against P501S-10E3-G4D3. Lane 1 is the biotinylated protein molecular weight marker (8 kDa).

Fig. 7

Figure 8. Mapping of the epitope recognized by 10E3-G4-D3

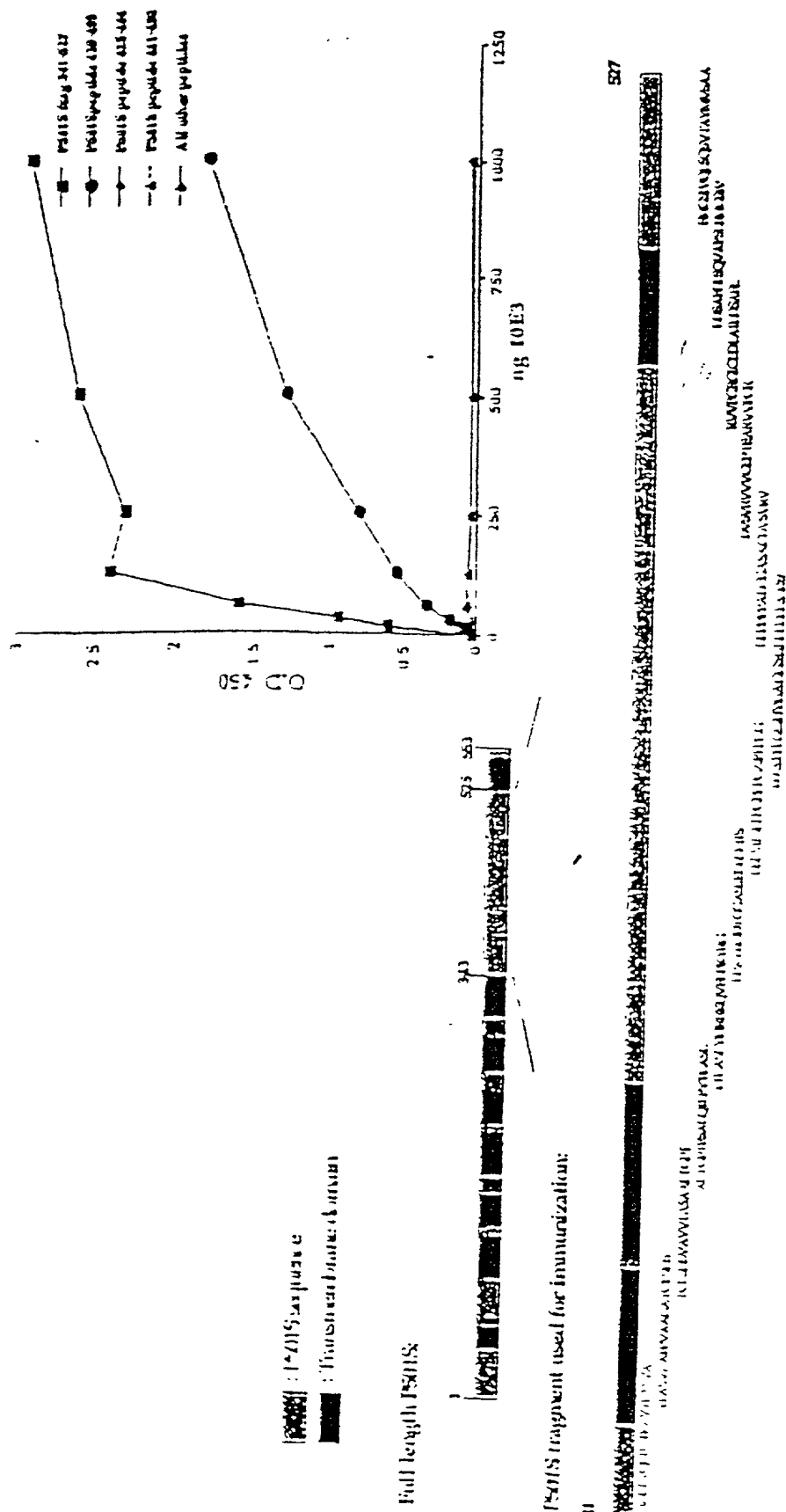


Fig. 8

7

Figure 1. Schematic of P501S with predicted transmembrane, cytoplasmic, and extracellular regions

MVQRLWYSRLIRKK AQLLLVNLTTGLFVCLAAQHTVVPFLLEVGVERKEN TNLVLGICPVLGLVCYPLLGSAS
 DHWRGGRYGRRRP EIWALSLGILLSLFLPRAGWL AGTCTDPRPLE LALLGLGVGLLDPCGQVCFIPL
 FALISMLFRDPDHCRQ AYSYVAFHSLGGCTGNTLPAL DAVDTSA LAPVLCGQFE
 CLPGLLTLPLLCVNAATLLY AFFVALGPTTPAPGLSAPVSLPHCTPQ RARLAFRNIGALLPRG
 HDLCCTAMPPTLRR LPYAFCLCSWMAIMTEFTFYIDP YGEGCLYQGVPRAPPGTEARRHYDEGVH
 MGSILGLFLQCAISLYPSLYM DRAVQREGTRAVYLAS YAAAPVAAAGATCLSHSVAVVTA SAA
 LTGHTFSALQILPYTLASLY HREKQVFLPKYRGDTGGASSEDSTMTSEFLPGPKPGAPFPNGHIVGAGGSGL
 LPPPPALCGASACDVSVRWVVGEPTEARVVVPGRG ELLDLALLDSAPFLSQVAPSLF MGSIVQLSQS
 VTAYMVSAAGILGLVAYFAT QVVFDKSDLAKYSA

Underlined sequence: Predicted transmembrane domain; Bold sequence: Predicted extracellular domain;
 Italic sequence: Predicted intracellular domain. Sequence in bold/underlined, used to generate polyclonal rabbit serum

Localization of domains predicted using HMMTOP (G.E. Tusnady and L. Simon (1998) Principles
 Governing Amino Acid Composition of Integral Membrane Proteins: Applications to topology Prediction. J.Mol Biol. 283,
 489-506.

Genomic Map of (5) Corixa Candidate Genes

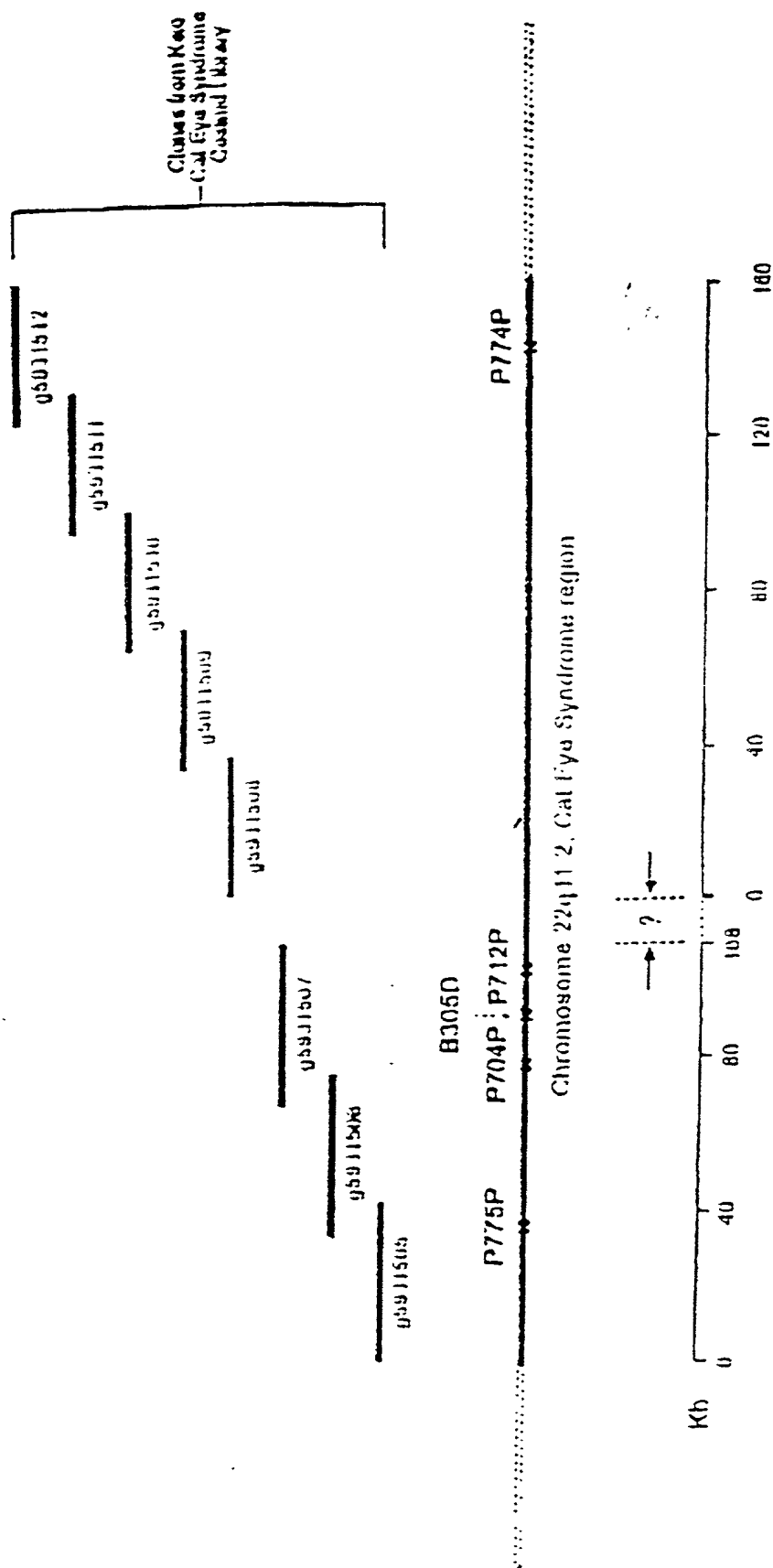


Fig. 10

FIGURE 4. Elisa assay of rabbit polyclonal antibody specificity

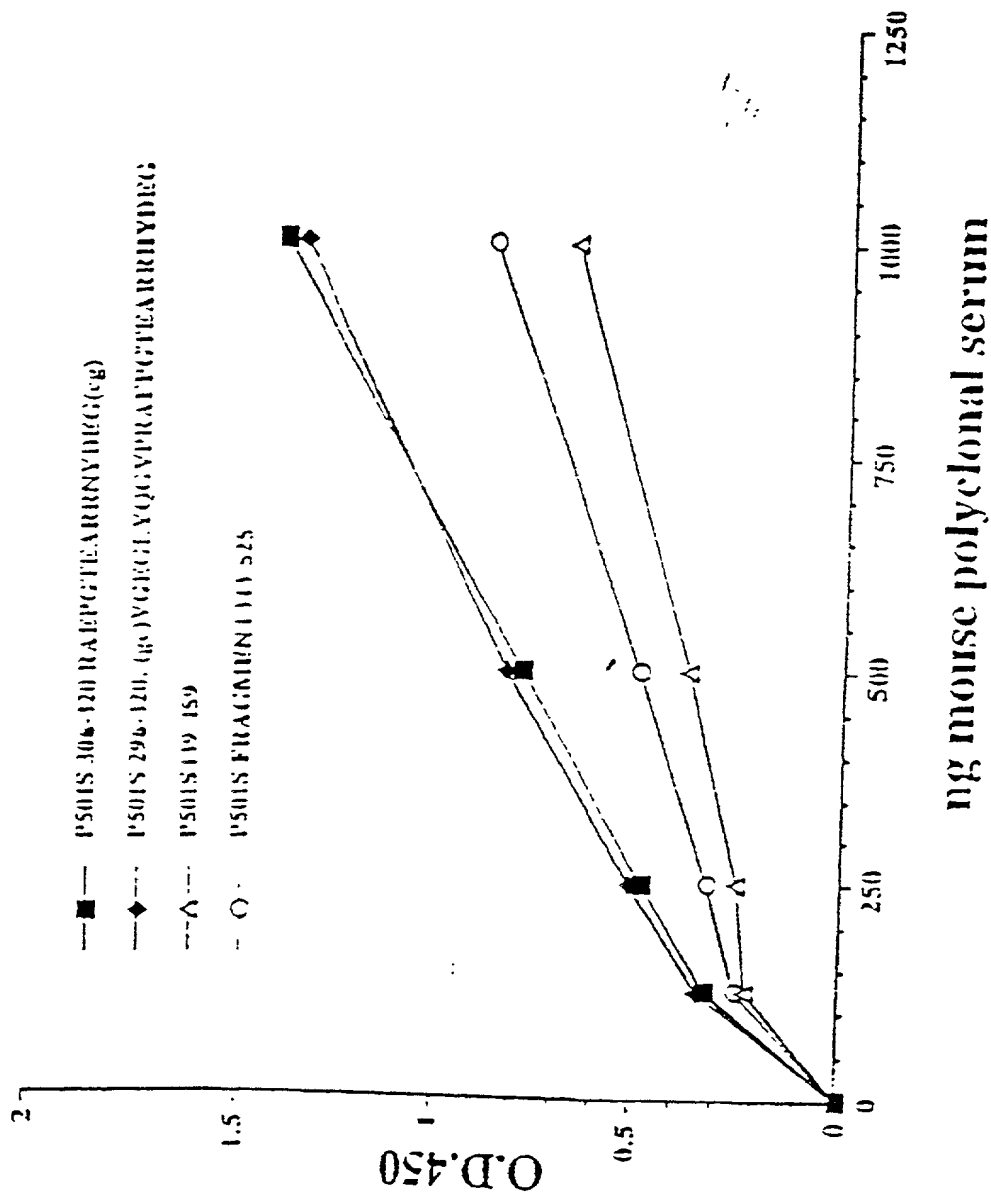


Fig. 11

10 20 30 40 50 60 70

GTCACCTTAGGAAAAGGTGTCTTTTCGGGCAGCCGGGCTCAGCATGAGGAACAGAAGGAATGACACTCTGG 70
ACAGCACCCGGACCCTGTACTCCAGCGCGTCTCGGAGCACAGACTTGTCTTACACTGAAAGCGACTTGGT 140
GAATTTTATTCAAGCAAATTTTAAGAAACGAGAATGTGTCTTCTTTACCAAAGATTCCAAGGCCACGGAG 210
AATGTGTGCAAGTGTGGCTATGCCAGAGCCAGCAGCATGGAAGGCACCCAGATCAACCAAAGTGAGAAAT 280
GGAACTACAAGAAACACACCAAGGAATTTCTACCGAGCCCTTTGGGGATATTTCAGTTTGAGACACTGGG 350

360 370 380 390 400 410 420

GAAGAAAGGGAGGTATATACGTCTGTCTCTGCGACACGGACGGGAAATCCTTTACGAGCTGCTGACCCAG 420
CACTGGCACCCTGAAAACAACCAACCTGGTCATTTCTGTGACCGGGGGCGCCAAGAACTTCGCCCTGAAGC 490
CGCGCATGCGCAAGATCTTCAGCCGGCTCATCTACATCGCGCAGTCCAAAGGTGCTTGGATTCTCACGGG 560
AGGCACCCATTATGGCCTGACGAAGTACATCGGGGAGGTGGTGAGAGATAACACCATCAGCAGGAGTTCA 630
GAGGAGAATATTGTGGCCATTGGCATAAGCAGCTGGGGCATGGTCTCCAAACGGGACACCCTCATCAGGA 700

710 720 730 740 750 760 770

ATTGCGATGCTGAGGGCTATTTTTTAGCCCAAGTACCTTATGGATGACTTCACAAGGGATCCACTGTATAT 770
CCTGGACAACCAACCACACACATTTGGCTGCTGGTGGACAATGGCTGTGATGGACATCCCACTGTGGAAGCA 840
AAGCTCCGGGAATCAGCTAGAGAAGCATATCTCTGAGCGCACTATTCAAGATTCCAACTATGGTGGCAAGA 910
TCCCCATTGTGTGTTTGGCCAAAGGAGGTGGAAAAGAGAGCTTTGAAAGCCATCAATACCTCCATCAAAAA 980
TAAAATTCTTGTGTGGTGGTGGGAAGGCTCGGGCGGATCGCTGATGTGATCGCTAGCCTGGTGGAGGTG 1050

1060 1070 1080 1090 1100 1110 1120

GAGGATGCCCGACATCTTCTSCCGTCAAGGAGAAGCTGGTGGCTTTTTTACCCCGCACGGTGTCTCGG 1120
TGCTTGAGGAGGAGACTGAGAGTTGGATCAAAATGGCTCAAGAAATTTCTCGAATGTTCTCACCTATTAAC 1190
TAGTTATTAAATGGAAGAAGCTGGGGATGAAATGTGAGCAATGCCATCTCTACGCTCTATACAAAAGCC 1260
TTTCAGCACCAAGTGAGCAAGACAAGGATAAAGTGGAAATGGGC-GCTGAAGCTCTTCTGGAGTGGAAACAGC 1330
TGGACTTAGCCCAATGATGAGATTTTACCAATGACCGCGATGGAGTCTGCTGACCTCAAGAAATCAT 1400

1410 1420 1430 1440 1450 1460 1470

GTTTACGGCTCTCATAAAGGACAGACCCAAAGTTGTCCGCTCTTTCTGGAGAATGGCTTGAACCTACGG 1470
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TGCAGATCGCCAAGAAATTCCTATAATGATGCCCTCTCACGTTTGTCTGGAAACTGGTTGCGAACTTCCG 1610
AAGAGGCTTCGGGAAGGAAGACAGAAATGGCGGGGAGAGATGGACATAGAAGCTCCACGACGTGTCTCT 1680
ATTACTCGGCACCCCTGCAAGCTCTCTTCATCTGGGCCATTCTTCAGAAAGAAGGAAGCTCTCCAAAG 1750

1760 1770 1780 1790 1800 1810 1820

TCATTTGGGAGCAGACCAAGGGCTGCACTCTGSCAGCCCTGCGAAGCAAGCTTCTGAAGACTCTGGC 1820
CAAAGTGAAGAACGACATCAATGCTGCTGGGGAGTGGAGGAGCTGGCTAATGAGTACGAGACCCGGGCT 1890
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Fig. 12A (i)

006230-921550

2110	2120	2130	2140	2150	2160	2170
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GGTCTTCTACATCGCTTCTCTCTGTGTTGCCACGTGCTGCTCATGGATTTCCATTCCGTGCCACAC	2310					
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2460	2470	2480	2490	2500	2510	2520
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CGTGGCCAGGCAAGGGATCCTTAGGCAGAAAGAGCAGCGCTGGAGGTGGATATTCGGTTCCGTATCTAC	2730					
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GTCGCCATGTTTGGCTACACGGTGGGCACCGTCCAGGAGAAACAATGACCAGGTCTGGAAGTCCAGAGGT	3010					
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3160	3170	3180	3190	3200	3210	3220
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CAAGGGTCTTCTGAAAAGAGATTGCTAATAAAATCAAAATAAACTGTATGAACTTETAATGAGAGAAAATC	3360					
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3510	3520	3530	3540	3550	3560	3570
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TTGATCATGGGATGAGCATCTTTGTGATGAATCTTATGCTGTATTTGGGAAAAATTTCCAAAGGTTAG	4480					
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Fig. 12A(2)

4560	4570	4580	4590	4600	4610	4620
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AAGAATTGCTGGAACCTGGGAGGCGGAGGTTGCAGTGAACCAAGATTGCACCACTGCCTCCAGCCGGGG						4900
4910	4920	4930	4940	4950	4960	4970
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AAGTGGTGGTATTTGAGCAGGATGTGCACAAGGCAATTGAAATGCCATAATTAGTTTCTCAGCTTTGAA						5110
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5260	5270	5280	5290	5300	5310	5320
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GTCAAA						5668

006280" 5521550

Fig. 12A(3)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : Jiangchun Xu et al.
Filed : August 29, 2000
For : COMPOSITIONS AND METHODS FOR THE THERAPY AND
DIAGNOSIS OF PROSTATE CANCER

Docket No. : 210121.427C18

Date : August 29, 2000

Box Patent Application
Assistant Commissioner for Patents
Washington, D.C. 20231

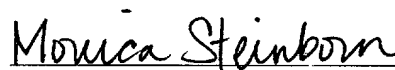
DECLARATION

Sir:

I, Monica Steinborn, in accordance with 37 C.F.R. § 1.821(f) do hereby declare that, to the best of my knowledge, the content of the paper entitled "Sequence Listing" and the computer readable copy contained within the floppy disk are the same.

I declare further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Dated this 29th day of August, 2000.



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006230 " 9E2T990

SEQUENCE LISTING

<110> Xu, Jiangchun
 Dillon, Davin C.
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 Harlocker, Susan L.
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 Henderson, Robert A.
 Kalos, Michael D.
 Fanger, Gary R.
 Retter, Marc W.
 Stolk, John A.
 Day, Craig H.
 Vedvick, Thomas S.
 Carter, Darrick
 Li, Samuel
 Wang, Aijun
 Skeiky, Yasir A.W.
 Hepler, William

<120> COMPOSITIONS AND METHODS FOR THE THERAPY AND
 DIAGNOSIS OF PROSTATE CANCER

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ctccttggct	cacagccttc	tctaggtctc	ccagtgcctc	caggacagag	tgggttatgt	240
tttcagctcc	atccttgctg	tgagtgtctg	gtgcgtttgtg	cctccagctt	ctgctcagtg	300
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ctagagcggc	cgccaccgcg	gtggagctcc	agcttttgtt	cccttttagtg	agggttaatt	420
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anctaactca cattaattgc gttgcgctca ctgnccgctt tccagtcngg aaaactgtcg      600
tgccagctgc attaatgaat cggccaacgc ncgggggaaaa gcggtttgcg ttttgggggc      660
tcttcgctt ctcgctcact nantcctgcg ctcggtcntt cggctgcggg gaacgggtatc      720
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aaggaacggg gctcgtttat caccagttag gagcaggacg tgagcccccg ccttgcacct      360
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ccaattcgcc ctatantgag tcgtattacg cgcgctcact ggccgctcgt ttacaacgct      480
gtgactggga aaaccctggg cgttaccac ttaatcgctc tgcagcacat ccccttttcg      540
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gaatgggnaa atgggacccc cctgttaccg cgcattnaac ccccgcnngg tttngttgtt 660
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cttcccttcc tttcncncn ctttcccccg ggggtttcccc cntcaaacc cna 773

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<212> DNA
<213> Homo sapien

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<223> n = A,T,C or G

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tgaagtaaatt ctagccatgc ttttaaaaaa tgcttttaggt cactccaagc ttggcagtta 240
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gggaananc	ctcgnccntn	ccccnttaa	tccncccttg	cnangnnctn	ccccnntcc	720
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<212> DNA
 <213> Homo sapien
 <220>
 <221> misc_feature
 <222> (1)...(789)
 <223> n = A,T,C or G

<400> 10
 cagtctatnt ggccagtgtg gcagctttcc ctgtggctgc cgggtgccaca tgcctgtccc 60
 acagtgtggc cgtggtgaca gcttcagccg ccctcaccgg gttcaccttc tcagccctgc 120
 agatcctgcc ctacacactg gcctccctct accaccggga gaagcagggtg ttcctgcccc 180
 aataccgagg ggacactgga ggtgctagca gtgaggacag cctgatgacc agcttcctgc 240
 cagggccctaa gcctggagct cccttcctta atggacacgt ggggtgctgga ggcagtggcc 300
 tgctcccacc tccaccgcg ctctgcgggg cctctgcctg tgatgtctcc gtacgtgtgg 360
 tgggtgggtga gccaccgan gccagggtgg ttccggggccg gggcatctgc ctggacctcg 420
 ccatcctgga tagtgcttcc tgctgtccca ngtggcccca tccctgttta tgggtctccat 480
 tgtccagctc agccagtctg tcaactgccta tatggtgtct gccgcaggcc tgggtctggt 540
 cccatttact ttgctacaca ggtantattt gacaagaacg anttggccaa atactcagcg 600
 ttaaaaaatt ccagcaacat tgggggtgga aggcctgcct cactgggtcc aactccccgc 660
 tctgttaaac cccatggggc tgccggcttg gccgccaaat tctgttgctg ccaaantnat 720
 gtggctctct gctgccacct gttgctggct gaagtgenta cngcncanct nggggggtng 780
 gngttccc 789

<210> 11
 <211> 772
 <212> DNA
 <213> Homo sapien
 <220>
 <221> misc_feature
 <222> (1)...(772)
 <223> n = A,T,C or G

<400> 11
 cccaccctac ccaaatatta gacaccaaca cagaaaagct agcaatggat tcccttctac 60
 tttgttaaat aaataagtta aatattttaa tgccctgtgtc tctgtgatgg caacagaagg 120
 accaacaggc cacatcctga taaaaggtaa gaggggggtg gatcagcaaa aagacagtgc 180
 tgtgggctga ggggacctgg ttcttgtgtg ttgcccctca ggactcttcc cctacaaata 240
 actttcatat gttcaaatcc catggaggag tgtttcatcc tagaaactcc catgcaagag 300
 ctacattaaa cgaagctgca ggttaagggg cttanagatg ggaaaccagg tgactgagtt 360
 tattcagctc ccaaaaaccc ttctctaggt gtgtctcaac taggaggcta gctgttaacc 420
 ctgagcctgg gtaatccacc tgcagagtcc ccgcattcca gtgcatggaa cccttctggc 480
 tccctgtat aagtccagac tgaaaccccc ttggaaggnc tccagtcagg cagccctana 540
 aactggggaa aaaagaaaag gacgccccan ccccagctg tgcanctacg cacctcaaca 600
 gcacagggtg gcagcaaaaa aaccacttta ctttggcaca aacaaaaact ngggggggca 660
 accccggcac cccnangggg gttaacagga ancngggnaa cntggaaccc aattnaggca 720
 ggcccnccac cccnaatntt gctgggaaat ttttctccc ctaaattntt tc 772

<210> 12
 <211> 751
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(751)
 <223> n = A,T,C or G

<400> 12
 gcccccaattc cagctgccac accacccacg gtgactgcat tagttcggat gtcatacaaaa 60
 agctgattga agcaaccctc tacttttttg tegttagcct tttgcttggt gcaggtttca 120
 ttggctgtgt tggtagcgtt gtcattgcaa cagaatgggg gaaaggcact gttctctttg 180
 aagtanggtg agtcctcaaa atccgtatag ttggtgaagc cacagcactt gagccctttc 240
 atggtggtgt tccacacttg agtgaagtct tcctgggaac cataatcttt cttgatggca 300
 ggcactacca gcaacgtcag ggaagtgtct agccattgtg gtgtacacca aggcgaccac 360
 agcagctgcn acctcagcaa tgaagatgan gaggangatg aagaagaacg tcncgagggc 420
 acacttgctc tcagtcttan caccatanca gcccntgaaa accaananca aagaccacna 480
 cncggctgc gatgaagaaa tnaccccneg ttgacaaact tgcattggcag tggganccac 540
 agtggccna aaaatcttca aaaaggatgc cccatcnatt gaccccccaa atgcccactg 600
 ccaacagggg ctgccccacn cncnnaacga tgancnatt gnacaagatc tncntggtct 660
 tnatnaacnt gaacctgcn tngtggtctc tgttcaggnc cnnngcctga cttctnaann 720
 aangaactcn gaagncccca cngganann g 751

<210> 13
 <211> 729
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(729)
 <223> n = A,T,C or G

<400> 13
 gagccaggcg tccctctgcc tgcccactca gtggcaacac ccgggagctg ttttgtcctt 60
 tgtggancct cagcagtncc ctctttcaga actcantgcc aagancctg aacaggagcc 120
 accatgcagt gcttcagctt cattaagacc atgatgatcc tcttcaattt gctcatcttt 180
 ctgtgtggtg cagccctgtt ggcagtgggc atctgggtgt caatcgatgg ggcacacctt 240
 ctgaagatct tcgggccact gtcgtccagt gccatgcagt ttgtcaacgt gggctacttc 300
 ctcacgcag ccggcgcttg ggtcttagct ctaggtttcc tgggctgcta tgggtgctaag 360
 actgagagca agtgtgccct cgtgacgttc ttcttcaccc tctctctcat cttcattgct 420
 gaggttgcaa tgctgtggtc gccttggtgt acaccacaat ggctgagcac ttcttgacgt 480
 tgctggtaat gcctgccatc aanaaaagat tatgggttcc cagggaanact tcaactcaagt 540
 gttggaacac caccatgaaa gggctcaagt gctgtggctt cncccaacta tacggatttt 600
 gaagantcac ctacttcaaa gaaaanagtg cctttccccc atttctgttg caattgacaa 660
 acgtcccaa cacagccaat tgaaaacctg caccacaacc aaangggctc ccaaccanaa 720
 attnaaggg 729

<210> 14
 <211> 816
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(816)
 <223> n = A,T,C or G

```
<210> 15
<211> 783
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(783)
<223> n = A,T,C or G
```

```
<210> 16
<211> 801
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(801)
<223> n = A,T,C or G
```

<400> 16

```

gccccaatc cagctgccac accaccacg gtgactgcat tagttcggat gtcatacaaa      60
agctgattga agcaaccctc tacttttttg tcgtgagcct tttgcttggt gcaggtttca    120
ttggctgtgt tgggtgacgtt gtcattgcaa cagaatgggg gaaaggcact gttctctttg    180
aagtaggggtg agtcctcaaa atccgtatag ttggtgaagc cacagcactt gagccctttc    240
atgggtgggtg tccacacttg agtgaagtct tcctgggaac cataatcttt cttgatggca    300
ggcactacca gcaacgtcag gaagtgtcga gccattgttg tgtacaccaa ggcgaccaca    360
gcagctgcaa cctcagcaat gaagatgagg aggaggatga agaagaacgt cncgagggca    420
cacttgctct ccgtcttagc accatagcag cccangaaac caagagcaaa gaccacaacg    480
ccngctgcga atgaaagaaa ntaccacgt tgacaaactg catggccact ggacgacagt    540
tggcccgaa atcttcagaa aagggatgcc ccattgattg aacaccana tgcccactgc    600
cnacagggct gcnccnncn gaaagaatga gccattgaag aaggatcntc ntggctcttaa    660
tgaactgaaa ccntgcatgg tggccctgt tcagggctct tggcagtga ttctganaaa    720
aaggaacngc ntnagcccc ccaaangana aaacaccccc ggggtgttgcc ctgaattggc    780
ggccaaggan ccctgccccn g                                     801

```

```

<210> 17
<211> 740
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(740)
<223> n = A,T,C or G

```

```

<400> 17
gtgagagcca ggcgtccctc tgctgcccc ctcagtggca acacccgga gctgttttgt      60
cctttgtgga gcctcagcag ttccctcttt cagaactcac tgccaagagc cctgaacagg    120
agccaccatg cagtgtctca gcttcattaa gaccatgatg atcctcttca atttgctcat    180
ctttctgtgt ggtgcagccc tgttggcagt gggcatctgg gtgtcaatcg atggggcatc    240
ctttctgaag atcttcgggc cactgtcgtc cagtgccatg cagtttgtca acgtgggcta    300
cttctcatc gcagccggcg ttgtggtctt tgctcttggt ttcttgggct gctatgggtgc    360
taagacggag agcaagtgtg ccctcgtgac gttcttcttc atcctcctcc tcctcttcat    420
tgctgaagtt gcagctgctg tggtcgcctt ggtgtacacc acaatggctg aaccattcct    480
gacgttgctg gtantgctg ccatcaanaa agattatggg ttcccaggaa aaattcactc    540
aantntggaa caccnccatg aaaagggctc caatttctgn tggcttcccc aactataccg    600
gaattttgaa agantcnccc tacttccaaa aaaaaanant tgccttttnc cccnttctgt    660
tgcaatgaaa acntcccaan acngccaatn aaaacctgcc cnnncaaaaa ggntcncaaa    720
caaaaaaant nnaagggttn                                     740

```

```

<210> 18
<211> 802
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(802)
<223> n = A,T,C or G

```

```

<400> 18
ccgctgggtg cgctgggtcca gngnagccac gaagcacgtc agcatacaca gcctcaatca      60
caaggtcttc cagctgccgc acattacgca gggcaagagc ctccagcaac actgcatatg    120
ggatacactt tacttttagca gccaggggtga caactgagag gtgtcgaagc ttattcttct    180

```



```

gagcctctgt tagtggagga agattccggg cttcagctaa gtagtcagcg tatgtcccat 240
aagcaaacac tgtgagcagc cggaaggtag aggcaaagtc actctcagcc agctctctaa 300
cattgggcat gtccagcagt tctccaaaca cgtagacacc agnggcctcc agcacctgat 360
ggatgagtgt ggccagcgct gcccccttgg ccgacttggc taggagcaga aattgctcct 420
ggttctgccc tgtcaccttc acttcgcgac tcatactgac actgagtgtg ggggacttgg 480
gctcaggatg tccagagacg tggttccgcc cctcncctta atgacaccgn ccanncaacc 540
gtcggctccc gccgantgng ttcgctgtn cttgggtcagg gtctgctggc cnetacttgc 600
aancttcgtc nggccccatgg aattcacenc accggaactn gtangatcca ctntttctat 660
aaccgngcgc caccgcnnnt ggaactccac tcttnttnc tttacttgag ggttaaggtc 720
acccttnncg ttaccttggg ccaaaccntn cctgtgtgctg anatngtnaa tcnggncna 780
tnccanccnc atangaagcc ng 802

```

```

<210> 19
<211> 731
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(731)
<223> n = A,T,C or G

```

```

<400> 19
cnaagcttcc aggtnacggg ccgcnaance tgaccenagg tancanaang cagncngcgg 60
gagcccaccg tcacngngng gngtctttat nggagggggc ggagccacat cnetggacnt 120
cntgaccca actcccncc nncantgca gtgatgagtg cagaactgaa ggtnacgtgg 180
caggaaccaa gancaaannc tgctccnntc caagtccgcn nagggggcgg ggctggccac 240
gncatccnt cnagtgtgn aaagcccn nctgtctact tgtttggaga acngcnnga 300
catgcccagn gttanataac nggcngagag tnantttgcc tctcccttcc ggctgcgcan 360
cngtntgtct tagnggacat aacctgacta cttaactgaa ccnngaate tncnccct 420
ccactaagct cagaacaaaa aacttcgaca ccactcantt gtcacctgnc tgctcaagta 480
aagtgtaccc catncccaat gtntgctnga ngctctgncc tgcnttangt tcggtcctgg 540
gaagacctat caattnaagc tatgtttctg actgcctctt gctccctgna acaancnacc 600
cnnnntcca agggggggnc ggcccccaat ccccccaacc ntnaattnan tttancccn 660
ccccnggcc cggcctttta cnancntcnn nnacngggna aaaccnnngc tttncccaac 720
nnaatccnc t 731

```

```

<210> 20
<211> 754
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(754)
<223> n = A,T,C or G

```

```

<400> 20
tttttttttt tttttttttt taaaaacccc ctccattnaa tgnaaacttc cgaaattgtc 60
caaccccttc ntccaaatnn ccntttccgg gnggggggttc caaacccaan ttanntttgg 120
annttaaatt aaatnttnnt tggnggnna anccnaatgt nangaaagtt naaccanta 180
tnancttnaa tncctggaaa ccngtngntt ccaaaaatnt ttaaccctta antccctccg 240
aaatngttna nggaaaaccc aanttctcnt aagggtgttt gaaggntnaa tnaaaanccc 300
mnccaattgt ttttngccac gcctgaatta attggnttcc gntgttttcc nttaaaanaa 360

```

```

ggnnancccc gggtantnaa tccccccnnc cccaattata ccganttttt ttngaattgg 420
gancccnccg gaattaacgg ggnnnnntccc tnttgggggg cnggnncccc ccccntcggg 480
gggtnggggnc aggnccnnaat tggtttaaggg tccgaaaaat ccctccnaga aaaaaanctc 540
ccaggntgag nntnggggttt nccccccccc cangggccct ctcgnaaggt tgggggtttgg 600
ggggcctggg attttntttc cctntttnc tccccccccc ccnggganag aggttngngt 660
tttgntcnnc ggccccnccn aaganctttt ccganttnan ttaaatecnt gcctnggcga 720
agtcctttgn agggntaaan ggccccctnn cggg 754

```

```

<210> 21
<211> 755
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(755)
<223> n = A,T,C or G

```

```

<400> 21
atcancccat gaccccnac nngggacnc tcanccggnc nnncnaccnc cgcccnatca 60
nngtnagnnc actncnnttn natcaacccc cncnactac gcccncnanc cnacgcnccta 120
nncanatncc actganngcg cganngtngan ngagaaanct nataccanag ncaccanacn 180
ccagctgtcc nanaangcct nnnatacngg nnnatccaat ntgnancctc cnaagtattt 240
nncnncanac gattttccctn anccgattac centncccc tancctctcc cccccaacna 300
cgaaggcnct ggncncaagg nngcgnccnc ccgctagntc ccnncnaagt cncncnccta 360
aactcanccn nattacnccg ttentgagta tcaactcccg aatctcacc tactcaactc 420
aaaaanatch gatacaaaat aatncaagcc tgnttatnac actntgactg ggtctctatt 480
ttagnngtcc ntnaancntc ctaatacttc cagtctncct tcnccaattt ccnaanggct 540
ctttcngaca gcatnttttg gttcccnntt ggggttcttan ngaattgcc ttentngaac 600
gggctctct tttccttcgg ttancctggg ttenncggc cagttattat ttcctntttt 660
aaattctnnc cntttanttt tggenttcna aacccccggc cttgaaaacg gccccctggt 720
aaaagggtgt tttganaaaa tttttgtttt gttcc 755

```

```

<210> 22
<211> 849
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(849)
<223> n = A,T,C or G

```

```

<400> 22
tttttttttt tttttangtg tngtcgtgca ggtagaggct tactacaant gtgaanacgt 60
acgctnggan taangcgacc cganntctag gannccctt aaaatcanac tgtgaagatn 120
atcctgnnna cggaanggtc accggnggat nntgctaggg tgncnctcc cannncttn 180
cataactcng nggccctgcc caccaccttc ggcggcceng ngncggggcc cgggtcattt 240
gnnttaaccn cactnngcna ncggtttccn nccccnngc acccnggcga tccgggggtnc 300
tctgtcttcc cctgnagncn anaaantggg ccnccgnccc ctttaccctt nnacaagcca 360
cngccttcta nccnccgccc cccctccant nngggggact gccnanngct ccgttctctg 420
nnaccccnnn gggtnccctg gttgtcgant cnaccgnang ccanggatc cnaaggaagg 480
tgcgttnttg gccctaccc ttgcctnccg nncaccttc ccgacnanga nccgctccc 540
cncnccgng cctcncctcg caacacccgc nctentcngt ncggnnnccc cccacccgc 600

```

```

nccctcncnc ngncgnannc ctcncncnc gtctcannca ccaccccgcc ccgccaggcc 660
ntcanccacn ggnngacnng nagnncnntc gcnccgcgcg gcgnncncct cgcncngaa 720
ctnctcngg ccantnncgc tcaanccnna cnaaacgcgc ctgcgcggcc cgnagcgncc 780
ncctccncga gtcctcccgn ctcccnaccc angnnttcn cgaggacacn nnaccccgcc 840
nncangcgg 849

```

```

<210> 23
<211> 872
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(872)
<223> n = A,T,C or G

```

```

<400> 23
gcgcaaacta tacttcgctc gnactcgtgc gcctcgtcnc tcttttcctc cgcaaccatg 60
tctgacnanc ccgattnggc ngatatcnan aagntcganc agtccaaact gantaacaca 120
cacacncnan aganaaatcc nctgccttcc anagtanacn attgaacnng agaaccangc 180
nggcgaatcg taatnaggcg tgcgcgcgca atntgtcncc gtttatntn ccagcntcnc 240
ctnccnacc tacntcttcn nagctgtcnn acccctngtn cgnaccccc naggtcggga 300
tcgggtttnn nntgaccgng cnnccctcc cccctccat nacganccnc ccgcaccacc 360
nanngcncgc nccccgnct cttegcncnc ctgtcctntn cccctgtngc ctggcncngn 420
accgcattga ccctcgcncn ctncnngaaa ncgnanacgt ccgggttggn annancgctg 480
tgggnnngcg tctgcncgc gtcccttcn nonncttcca ccctcttct tacngggtct 540
cncgcctc tcnnncaac cctgggaacg tntcctntgc ccccttnac tccccctt 600
cgnctgnc cgnccccacc ntcatttnca nacgntcttc acaannncct ggntnncctc 660
cnancngncn tcancncnag ggaagggngg ggnnccnntg nttgacgttg ngngangtc 720
cgaanantcc tcncntcan cncctaccct cgggcgnct ctngttnc aacttancaa 780
ntctcccccg ngngcncntc tcagcctcnc cccccnct ctctgcantg tncctcgtc 840
tnaccnntac gantnttcn cncctcttt cc 872

```

```

<210> 24
<211> 815
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(815)
<223> n = A,T,C or G

```

```

<400> 24
gcatgcaagc ttgagtattc tatagngtca cctaaatanc ttggcntaat catggtcnta 60
nctgncttcc tgtgtcaaata gtatacnaan tanatatgaa tctnatntga caaganngta 120
tctnctatta gtaacaantg tnntgtccat cctgtengan canattccca tnnattncgn 180
cgcattcncn gncantatn taatngggaa ntcnnntnnn ncaccnncat ctatcntncc 240
gnccttgac tggagagat ggatnanttc tnntntgacc nacatgttca tcttgattn 300
aanaccccc cgcngnccac cggttngng cnagcncntc ccaagacctc ctgtggaggt 360
aacctgcgtc aganncatca aacntgggaa accgcncnc angtnnaagt ngnnncanan 420
gatcccgctc aggnntnacc atcccttcnc agcgccttct tngtgcctt anagnnagc 480
gtgtccnanc cncatcaat ganacgcgc agnccanccg caattnggca caatgtcgnc 540
gaacccccca gggggantna tncaaanccc caggattgtc cncncangaa atccncanc 600

```

```

ccnccctac ccnctttgg gacngtgacc aantcccga gtnccagtcc ggcngnctc 660
ccccaccggt nncntgggg ggggtgaanct cngnntcanc cngncgaggn ntcgnaagga 720
accggncctn ggcgaanng ancnnctnga agngccnct cgtataacct cccctcncca 780
nccnacngnt agntcccccc cngggtnccg aangg 815

```

```

<210> 25
<211> 775
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(775)
<223> n = A,T,C or G

```

```

<400> 25
ccgagatgtc tcgctccgtg gccttagctg tgctcgcgct actctctctt tctggcctgg 60
aggctatcca gcgtactcca aagattcagg ttactcacg tcatccagca gagaatggaa 120
agtcaaattt cctgaattgc tatgtgtctg ggtttcatcc atccgacatt gaanttgact 180
tactgaagaa tgganagaga attgaaaaag tggagcattc agacttgtct ttcagcaagg 240
actggtcttt ctatctcntg tactacactg aattcacccc cactgaaaaa gatgagtatg 300
cctgccgtgt gaaccatgtg actttgtcac agcccaagat agttaagtgg gatcgagaca 360
tgtaagcagn cnnatggaa gtttgaagat gccgcatttg gattggatga attccaaatt 420
ctgcttgctt genttttaat antgatatgc ntatacacc taccctttat gnccccaaatt 480
tgtaggggtt acatnantgt tcnentngga catgatcttc ctttataant cncnnttcg 540
aattgcccggt cncncngttn ngaatgtttc cnaaaccacg gttggctccc ccaggtcncc 600
tcttacggaa gggcctgggc cnccttncaa ggttggggga accnaaaatt tcncttntgc 660
cncnccncca cnnctctgng nncncanttt ggaacccttc cnattcccct tggcctcnna 720
nccttnncta anaaaacttn aaanccgtngc naaanntttn acttcccccc ttacc 775

```

```

<210> 26
<211> 820
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(820)
<223> n = A,T,C or G

```

```

<400> 26
anattantac agtghtaatct tttcccagag gtgtgtanag ggaacggggc ctagaggcat 60
ccanagata ncttatanca acagtgtttt gaccaagagc tgctgggcac atttcctgca 120
gaaaagggtg cggcccccat cactcctcct ctcccatagc catcccagag ggggtgagtag 180
ccatcangcc ttcggtgagg gggagtcang gaaacaacan accacagagc anacagacca 240
ntgatgacca tgggcgggag cgagcctctt ccctgnaccg ggggtggcana nganagccta 300
nctgaggggt cacactataa acgttaacga ccnagatnan cacctgcttc aagtgcaccc 360
ttcctacctg acnaccagn accnnaact gcngcctggg gacagcnctg ggancagcta 420
acnagcact cacctgcccc cccatggcgg tncgntccc tggctctgnc aagggaagct 480
ccctgttggg attncgggga naccaaggga nccccctcct ccantgtga aggaaaaann 540
gatggaattt tnccttccg gccnntcccc tcttcttta cagccccct nntactctc 600
tccctctntt ntcctgncnc acttttnacc ccnnnatttc ccttnattga tcggannctn 660
ganattccac tnnccgctnc cntcnatcng naanacnaaa nactntctna cccnggggat 720
gggnncctcg ntcacctct ctttttctc accnccnntt ctttgctct ccttngatca 780

```

tccaacntc gntggcentn ccccccnnn tcctttncce

820

<210> 27
 <211> 818
 <212> DNA
 <213> Homo sapien

 <220>
 <221> misc_feature
 <222> (1)...(818)
 <223> n = A,T,C or G

<400> 27
 tctgggtgat ggcctcttcc tctcagga cctctgactg ctctgggcca aagaatctct 60
 tgtttcttct ccgagcccca ggcagcgggtg attcagccct gcccaacctg attctgatga 120
 ctgcggatgc tgtgacggac ccaaggggca aatagggtcc cagggtccag ggaggggagc 180
 ctgctgagca ctcccgcccc tcacctgcc cagccctgc catgagctct gggctgggtc 240
 tccgcctcca gggttctgct ctccangca ngccancaag tggcgctggg ccacactggc 300
 ttcttctgct cccntccctg gctctgante tctgtcttcc tgcctgtgc angcnccttg 360
 gatctcagtt tccctcctc anngaactct gttctgann tcttcantta actntgantt 420
 tatnaccnan tggctgtnc tgcnnactt taatgggccc gaccggctaa tccctccctc 480
 nctcccttcc anttcnnnna accngcttnc cntctctcc cntancccg ccngggaanc 540
 ctcccttgcc ctnaccangg gccnnnaccg cccntnnctn ggggggcnng gtnnctnenc 600
 ctgntnnccc cncctcncnt tncctcgtcc cnnncnccn nngcannttc nengtcccn 660
 tnnctcttcn ngntcgnaa ngntcncntn tnnnnngnnc ngntnntnnc tccctctcnc 720
 cnnntgnang tnnntnnnnc ncngnncccc nnnncnnnnn nggnntnnn tctnncncg 780
 cccnncccc ngnattaagg cctcnnctc ccggccnc 818

<210> 28
 <211> 731
 <212> DNA
 <213> Homo sapien

 <220>
 <221> misc_feature
 <222> (1)...(731)
 <223> n = A,T,C or G

<400> 28
 aggaagggcg gagggatatt gtangggatt gagggatagg agnataangg gggaggtgtg 60
 tccaacatg anggtgnngt tctcttttga angaggggtg ngtttttann ccnggtgggt 120
 gattnaaccc cattgtatgg agnnaaagg tttnagggtat ttttcggctc ttatcagtat 180
 ntanattcct gtnaatcgga aaatnatnt tcnncnggaa aatnttgctc ccatccgnaa 240
 attnctcccg gtagtgcac nttngggggn cngccangtt tcccaggctg ctanaatcgt 300
 actaaagntt naagtggan tncaaatgaa aacctnnac agagnatccn taccgactg 360
 tnnntnctc tgcctctntg actctcngng agcccaatac ccnngngnat gtcnccngn 420
 nnngegnenc tgaaannnnc tcnnggctnn gancatcang gggtttcgca tcaaaagcnn 480
 cgtttcncat naaggcactt tngcctcatc caaccnctng cctcnncca tttngccgtc 540
 nggttcnct acgctnnntg cncctnnntn ganattttnc ccgctnggg naancctcct 600
 gnaatgggta gggncctntc ttttnaccnn gnggtntact aatcnnctnc acgctnctt 660
 tctnacccc ccccttttt caatcccanc ggcnaatggg gtctccccnn cgangggggg 720
 nnnccannc c 731

<210> 29

```

<211> 822
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(822)
<223> n = A,T,C or G

```

```

<400> 29
actagtccag tgtggtggaa ttccattgtg ttggggncnc ttctatgant antnttagat      60
cgctcanacc tcacancctc ccnaccnangc ctataangaa nannaataga nctgtncnnt      120
atntntacnc tcatanncct cnnnacccac tccctcttaa cccntactgt gcctatngcn      180
tnnctantct ntgcgcctn cnanccacn gtgggcnac cncnngnatt ctcnatctcc      240
tcnccatntn gcctananta ngtncatacc ctatacctac nccaatgcta nnnctaanch      300
tccatnantt annntaacta ccaactgacnt ngactttcnc atnanctcct aatttgaatc      360
tactctgact cccaengcct annnattagc ancntcccc nacnatntct caaccaaadc      420
ntcaacaacc tatctantctg ttncccaacc nttncctccg atccccnnac aacccccctc      480
ccaaataccc nccacctgac ncctaaccn caccatcccg gcaagccnan ggcattttan      540
ccactggaat cacnatngga naaaaaaac ccnaactctc tancncnnat ctccctaana      600
aatnctcctn naatttactn ncantnccat caanccacn tgaaacnnaa cccctgtttt      660
tanatccctt ctttcgaaaa ccnacccttt annncccaac ctttngggcc ccccnctnc      720
ccnaatgaag gncncccaat cnangaaacg nccntgaaaa ancnaggcna anannntccg      780
canatcctat cccttanttn ggggnccctt nccnggggcc cc                        822

```

```

<210> 30
<211> 787
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(787)
<223> n = A,T,C or G

```

```

<400> 30
cgccgcctg ctctggcaca tgccctcctga atggcatcaa aagtgatgga ctgccattg      60
ctagagaaga ccttctctcc tactgtcatt atggagccct gcagactgag ggctcccctt      120
gtctgcagga tttgatgtct gaagtcgtgg agtgtggcct ggagctcctc atctacatna      180
gctggaagcc ctggagggcc tctctcgcca gccctcccct tctctccacg ctctccangg      240
acaccagggg ctccaggcag cccattatct ccagnangac atgggtgtttc tccacgcgga      300
cccatggggc ctgnaaggcc aggggtctcct ttgacaccat ctctcccgtc ctgcctggca      360
ggccgtggga tccactantt ctanaacggn cgcacccncc gtgggagctc cagcttttgt      420
tccnttaat gaaggtaaat tgcncgcttg gcgtaacat nggtcanaac tntttcctgt      480
gtgaaattgt ttntccctc ncnattccnc ncnacatacn aaccgggaan cataaagtgt      540
taaagcctgg ggtngcctn nngaataaac tnaactcaat taattgcgtt ggctcatggc      600
ccgttttccn ttcnngaaaa ctgtcntccc ctgcnttnnt gaatcggccca ccccccnggg      660
aaaagcgggt tgcnttttng ggggntcctt ccncttcccc cctcnctaan cctnccgctt      720
cggtcgttnc nggtngcggg gaanggnat nnnctccncc naagggggng agnnngntat      780
ccccaaa

```

```

<210> 31
<211> 799
<212> DNA

```

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(799)

<223> n = A,T,C or G

<400> 31

tttttttttt	ttttttttggc	gatgctactg	tttaattgca	ggaggtgggg	gtgtgtgtac	60
catgtaccag	ggctattaga	agcaagaagg	aaggagggag	ggcagagcgc	cctgctgagc	120
aacaaaggag	tcctgcagcc	ttctctgtct	gtctcttggc	gcaggcacat	ggggaggcct	180
cccgcaagggt	ggggggccacc	agtccagggg	tgggagcact	acanggggtg	ggagtgggtg	240
gtggctggtn	cnaatggcct	gncacanatc	cctacgattc	ttgacacctg	gatttcacca	300
ggggaccttc	tgttctccca	nggnaacttc	ntnnatctcn	aaagaacaca	actgtttctt	360
cngcanttct	ggctgttcat	ggaaagcaca	ggtgtccnat	ttnggctggg	acttgggtaca	420
tatggttccg	gcccacctct	cccntcnaaa	aagtaattca	cccccccccn	ccntctnttg	480
cctgggccct	taantaccca	caccggaact	canttantta	ttcatcttng	gntgggcttg	540
ntnatcnccn	cctgaangcg	ccaagttgaa	aggccacgcc	gtncnccnctc	cccatagnan	600
ntttttnent	cantaaatgc	ccccccnggc	aacnatccaa	cccccccccn	tggggggccc	660
agcccanggc	ccccgnctcg	ggnnnccngn	cncgnantcc	ccaggntctc	ccantcngnc	720
ccnnngcncc	cccgcaagca	gaacanaagg	ntngagccnc	cgcannnnnn	nggtnnncnac	780
ctcgcccccc	ccnnccgngg					799

<210> 32

<211> 789

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(789)

<223> n = A,T,C or G

<400> 32

tttttttttt	tttttttttt	tttttttttt	tttttttttt	tttttttttt	tttttttttt	60
tttttncnag	ggcagggtta	ttgacaacct	cnogggacac	aancaggctg	gggacaggac	120
ggcaacaggc	tccggcgcg	gcggcgcgcg	ccctacctgc	ggtaccaa	ntgcagcctc	180
cgtccccgt	tgatnttct	ctgcagctgc	aggatgcct	aaaacagggc	ctcgccntn	240
ggtgggcacc	ctgggatttn	aattttccacg	ggcacaatgc	ggtcgcancc	cctcaccacc	300
nattaggaat	agtggtnnta	ccnccnccg	ttggcnca	ccccntggaa	accacttntc	360
gcggctccgg	catctgggtc	taaaccttgc	aaacnctggg	gccctctttt	tggttantnt	420
ncngccaca	atcatnactc	agactggcnc	gggctggccc	caaaaaancn	ccccaaaacc	480
ggnccatgtc	ttnnccgggt	tgtctgnatn	tncatcacct	cccgggcnc	ncaggncaac	540
ccaaaagttc	ttgnggccn	caaaaaanct	ccggggggnc	ccagtttcaa	caaagtcac	600
ccccttggcc	cccaaatcct	ccccccgntt	nctggggttg	ggaacccacg	cctctnnctt	660
tggnnggcaa	gntggntccc	ccttcggggc	cccgggtggc	ccnctctaa	ngaaaacncc	720
ntcctnnnca	ccatcccccc	nngnnacgnc	tancaangna	tccttttttt	tanaaacggg	780
ccccccnccg						789

<210> 33

<211> 793

<212> DNA

<213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(793)
 <223> n = A,T,C or G

<400> 33

gacagaacat	ggttgatggt	ggagcacctt	tctatacgac	ttacaggaca	gcagatgggg	60
aattcatggc	tggttgagca	atanaacccc	agttctacga	gctgctgac	aaaggacttg	120
gactaaagtc	tgatgaactt	cccaatcaga	tgagcatgga	tgattggcca	gaaatgaana	180
agaagtttgc	agatgtat	gcaaagaaga	cgaaggcaga	gtggtgtcaa	atctttgacg	240
gcacagatgc	ctgtgtgact	ccggttctga	cttttgagga	ggttgttcat	catgatcaca	300
acaangaacg	gggctcgttt	atcaccantg	aggagcagga	cgtgagcccc	cgccctgcac	360
ctctgctggt	aaacacccca	gccatccctt	ctttcaaaaag	ggatccacta	cttctagagc	420
ggncgccacc	gcggtggagc	tccagctttt	gttcccttta	gtgagggtta	attgcgcgct	480
tggcgtaatc	atggtcatan	ctgtttcctg	tgtgaaattg	ttatccgctc	acaattccac	540
acaacatacg	anccggaagc	atnaaatttt	aaagcctggg	ggtngcctaa	tgantgaact	600
nactcacatt	aattggcttt	gcgctcactg	cccgttttcc	agtcgggaaa	acctgtcctt	660
gccagctgcc	nttaatgaat	cnggccaccc	cccggggaaa	aggcngtttg	cttnttgggg	720
cgcncttccc	gctttctcgc	ttcctgaant	ccttcccccc	ggtctttcgg	cttgcggcna	780
acggtatcna	cct					793

<210> 34
 <211> 756
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(756)
 <223> n = A,T,C or G

<400> 34

gccgcgaccg	gcatgtacga	gcaactcaag	ggcgagtggg	accgtaaaaag	ccccaatctt	60
ancaagtgcg	gggaanagct	gggtcgactc	aagctagttc	ttctggagct	caacttcttg	120
ccaaccacag	ggaccaagct	gaccaaacag	cagctaattc	tggtcccgta	catactggag	180
atcgggggcc	aatggagcat	cctacgcaan	gacatcccct	ccttcgagcg	ctacatggcc	240
cagctcaaat	gctactactt	tgattacaan	gagcagctcc	ccgagtcagc	ctatatgcac	300
cagctcttgg	gcctcaacct	cctcttctctg	ctgtcccaga	accgggtggc	tgantnccac	360
acgganttgg	ancggctgcc	tgcccaanga	catacanacc	aatgtctaca	tcnaccacca	420
gtgtccttga	gcaatactga	tggtggcgag	ctaccncaaa	gtnttctctg	ccnagggtta	480
catccccgcg	cgagagctac	accttcttca	ttgacatcct	gctcgacact	atcagggatg	540
aaaatcgcn	ggttgctcca	gaaaggctnc	aanaanatcc	ttttcnctga	aggcccccg	600
atncnctagt	nctagaatcg	gcccgcacat	gcggtgganc	ctccaacctt	tcgttnccct	660
ttactgaggg	tttattgccc	cccttggcgt	tatcatggtc	acnccngttn	cctgtgttga	720
aattnttaac	cccccaaat	tccacgcna	cattng			756

<210> 35
 <211> 834
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(834)

<223> n = A,T,C or G

<400> 35

ggggatctct	anatcnacct	gnatgcatgg	ttgtcgggtgt	ggtcgctgtc	gatgaanatg	60
aacaggatct	tgcccttgaa	gctctcggct	gctgtnttta	agttgctcag	tctgccgtca	120
tagtcagaca	cnetcttggg	caaaaaacan	caggatntga	gtcttgattt	cacctccaat	180
aatcttcngg	gctgtctgct	cgggtgaactc	gatgacnang	ggcagctggg	tgtgtntgat	240
aaantccanc	angttctcct	tggtgacctc	cccttcaaag	ttgttccggc	cttcatcaaa	300
cttctnnaan	angannancc	cancctttgtc	gagctggnat	ttgganaaca	cgctactggt	360
ggaaactgat	cccaaattgg	atgtcatcca	tcgcctctgc	tgccctgcaa	aaacttgctt	420
ggcncaaate	cgactcccn	tccttgaaag	aagccnatca	cacccccctc	cctggactcc	480
nncaangact	ctnccgctnc	cccntccnng	cagggttggg	ggcannccgg	gcccntgcgc	540
ttcttcagcc	agttcacnat	nttcatcagc	ccctctgcc	gctgttntat	tccttggggg	600
ggaanccgtc	tctcccttcc	tgaannaact	ttgaccgtng	gaatagccgc	gcntcncnt	660
acntnctggg	ccgggttcaa	antccctcnc	ttgncnntcn	cctcggggcca	ttctggattt	720
nccnaacttt	ttccttcccc	cncctcncgg	ngtttggnnt	tttcatnggg	ccccaaactct	780
gctnttggcc	antcccttgg	gggcntntan	cncctcctnt	ggcc		834

<210> 36

<211> 814

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(814)

<223> n = A,T,C or G

<400> 36

cgngcgtttt	ccngccgcgc	cccgttttcca	tgacnaaggc	tcctttcang	ttaaatacnn	60
cctagnaana	attaatgggt	tgctctacta	atacatcata	cnaaccagta	agcctgcca	120
naacgccaac	tcaggccatt	cctaccaaag	gaagaaaggc	tggtctctcc	acccctgta	180
ggaaaggcct	gccttgtaag	acaccacaat	ncggctgaat	ctnaagtctt	gtgttttact	240
aatggaaaaa	aaaaataaac	aanagggtttt	gttctcatgg	ctgcccaccg	cagcctggca	300
ctaaaacanc	ccagcgctca	cttctgcttg	ganaaatatt	ctttgctctt	ttggacatca	360
ggcttgatgg	tatcactgcc	acntttccac	ccagctgggc	ncccttcccc	catntttgtc	420
antganctgg	aaggcctgaa	ncttagtctc	caaaagtctc	ngcccacaag	accggccacc	480
aggggangtc	ntttncagtg	gatctgccaa	anantaccen	tatcatcnnt	gaataaaaag	540
gcccctgaac	ganatgcttc	cancancctt	taagacccat	aatcctngaa	ccatgggtgcc	600
cttccgggtc	gatccnaaag	gaatgttcc	gggtcccant	ccctcctttg	ttnccttacgt	660
tgtnttggac	ccntgctngn	atnacccean	tganatcccc	ngaagcacc	tnccctggc	720
atttganttt	cntaaattct	ctgccctacn	nctgaaagca	cnattccctn	ggcncnnaan	780
ggngaactca	agaaggtctn	ngaaaaacca	cncn			814

<210> 37

<211> 760

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(760)

<223> n = A,T,C or G

<400> 37

```

gcacgtctgct cttcctcaaa gttgtttcttg ttgccataac aaccaccata ggtaaagcgg      60
gcgcagtgtt cgctgaaggg gttgtagtac cagcgcgagg tgctctcctt gcagagtcct      120
gtgtctggca ggtccacgca atgccctttg tccactggga aatggatgcg ctggagctcg      180
tcnaanccac tegtgtattht ttcacangca gcctcctccg aagcctccgg gcagttgggg      240
gtgtcgtcac actccactaa actgtcgatn cancagccca ttgctgcagc ggaactgggt      300
gggctgacag gtgccagaac acactggatn ggcttttcca tggaagggcc tgggggaaat      360
cncctnanc caaactgcct ctcaaaggcc accttgaca ccccgacagg ctagaaatgc      420
actcttcttc ccaaaggtag ttgttcttgg tgcccaagca ncctccanca aacccaaanc      480
ttgcaaaatc tgctccgtgg gggcatnnn taccanggtt ggggaaanaa acccgcnagn      540
ganccncctt gtttgaatgc naaggnaata atcctcctgt cttgcttggg tggaanagca      600
caattgaact gttaacnttg ggccngttc cncnnggtg gtctgaaact aatcacgcgc      660
actggaaaaa ggtangtgcc ttccttgaat tcccaaantt cccctngntt tgggtntttt      720
ctcctctncc ctaaaaatcg tnttcccccc cntangggc      760

```

<210> 38

<211> 724

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(724)

<223> n = A,T,C or G

<400> 38

```

tttttttttt tttttttttt tttttttttt tttttaaaaa cccctccat tgaatgaaaa      60
cttcnaaat tgtccaaccc cctcnccaa atnnccattt cggggggggg gttccaaacc      120
caaatttaatt ttgganttta aattaaatnt tnattngggg aanaanccaa atgtnaagaa      180
aatttaaccc attatnaact taaatnccn gaaaccntg gnttccaaaa atttttaacc      240
cttaaatccc tccgaaattg ntaanggaaa accaaattcn cctaaggctn tttgaagggt      300
ngatttaaac ccccttnant tnttttnacc cnngnctnaa ntatttngnt tccggtgttt      360
tcctnttaan cntnggtaac tcccgntaat gaannnccct aanccaatta aaccgaattt      420
tttttgaatt ggaaattccn ngggaattna cgggggtttt tccnttttg gggccatncc      480
ccncttttcg gggtttggn ntaggttgaa tttttnnang ncccaaaaaa ncccccaana      540
aaaaaactcc caagnnttaa ttngaantnc ccccttccca ggccttttg gaaaggnggg      600
ttntggggg cngggantt cnttcccccn ttncncccc cccccnggt aaanggttat      660
ngnntttggt ttttgggccc cttnanggac cttccggatn gaaattaaat ccccggnccg      720
gccg      724

```

<210> 39

<211> 751

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(751)

<223> n = A,T,C or G

<400> 39

```

tttttttttt tttttctttg ctcacattta atttttattht tgattttttt taatgctgca      60
caacacaata tttatttcat ttgtttcttt tatttcattt tatttgtttg ctgctgctgt      120
tttatttatt tttactgaaa gtgagaggga acttttgttg ccttttttcc tttttctgta      180

```

```

ggccgcctta agcttttctaa atttggaaca tctaagcaag ctgaanggaa aaggggggttt 240
cgcaaaatca ctcgggggaa nggaaagggtt gctttgttaa tcatgcccta tgggtgggtga 300
ttaactgctt gtacaattac ntttcacttt taattaattg tgctnaangc tttaattana 360
cttggggggtt ccctccccc accaaccnccn ctgacaaaaa gtgccngccc tcaaatnatg 420
tcccggcnnt cnttgaaaca cacngcngaa ngttctcatt ntcccnncnc caggtnaaaa 480
tgaagggtta ccatntttta cncacctcc acntggcnnn gcctgaatcc tcnaaaancn 540
ccctcaancn aattnctnng ccccggtcnc gcntnngtcc cncgggggtt ccggaantn 600
caccnccnga annnntnnc naacnaaatt ccgaaaatat tccnntcnc tcaattcccc 660
cnnagactnt cctcnncnan cncaattttc ttttnntcac gaacncgunc cnnaaaatgn 720
nnnncnctc cncnngtcn naatcnccan c 751

```

<210> 40

<211> 753

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(753)

<223> n = A,T,C or G

<400> 40

```

gtggtatttt ctgtaagatc aggtgttctt ccctcgtagg tttagaggaa acaccctcat 60
agatgaaaac ccccccgaga cagcagcact gcaactgcc aagcagccggg gtaggagggg 120
cgccctatgc acagctgggc ccttgagaca gcagggttc gatgtcaggc tcgatgtcaa 180
tgggtctggaa gggcgggctg tacctgcgta ggggcacacc gtcaggggccc accaggaact 240
tctcaaagtt ccaggcaacn tgggtgcgac acaccggaga ccagggtgatn agcttgggggt 300
cggtcataa cggcgggtggc tggctgcgtg gagctggcag ggcctcccg aggaaggcna 360
ataaaagggtg cggccccgca ccgttcnct cgcacttctc naanaccatg angttgggct 420
cnaaccacc accannccgg acttccttga nggaattccc aaatctcttc gntcttgggc 480
ttctnctgat gccctanctg gttgccnngn atgccaanca nccccancc ccgggggtcct 540
aaanaccncc cctcctcntt tcatctgggt tntntcccc ggacctgggt tctctcaag 600
ggancccata tctcnaccan tactcaacct nccccccnt gnnaccanc cttctanngn 660
tccccnccg nctctgggc cntcaaan gcttnacna cctgggtctg ccttcccccc 720
tncctatct gnaccnccn tttgtctcan tnt 753

```

<210> 41

<211> 341

<212> DNA

<213> Homo sapien

<400> 41

```

actatatcca tcacaacaga catgcttcat cccatagact tcttgacata gcttcaaagt 60
agtgaacca tccttgattt atatacatat atgttctcag tattttggga gcctttccac 120
ttctttaaac cttgttcatt atgaacactg aaaataggaa tttgtgaaga gtaaaaagt 180
tatagcttgt ttacgtagta agtttttgaa gtctacattc aatccagaca cttagttag 240
tgttaaactg tgatttttaa aaaatatcat ttgagaatat tctttcagag gtattttcat 300
ttttactttt tgattaattg tgttttatat attagggtag t 341

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<210> 42

<211> 101

<212> DNA

<213> Homo sapien

006230" 922590

<400> 42
 acttactgaa ttttagttctg tgctcttctt tatttagtgt tgtatcataa atactttgat 60
 gtttcaaaca ttctaaataa ataattttca gtggcttcat a 101

<210> 43
 <211> 305
 <212> DNA
 <213> Homo sapien

<400> 43
 acatctttgt tacagtctaa gatgtgttct taaatcacca ttccttctg gtcctcaccc 60
 tccaggggtg tctcacactg taattagagc tattgaggag tctttacagc aaattaagat 120
 tcagatgcct tgctaagtct agagttctag agttatgttt cagaaagtct aagaaaccca 180
 cctcttgaga ggtcagtaaa gaggacttaa tatttcatat ctacaaaatg accacaggat 240
 tggatacaga acgagagtta tcttgataa ctcagagctg agtacctgcc cgggggccgc 300
 tcgaa 305

<210> 44
 <211> 852
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(852)
 <223> n = A,T,C or G

<400> 44
 acataaatat cagagaaaag tagtctttga aatatttacg tccaggagtt ctttgtttct 60
 gattatttgg tgtgtgtttt gggttgtgtc caaagtattg gcagcttcag ttttcatttt 120
 ctctccatcc tcgggcattc ttcccaaatt tatataccag tcttcgtcca tccacacgct 180
 ccagaatttc tctttttagt taatatctca tagctcggct gagcttttca taggtcatgc 240
 tgctgttgtt cttcttttta ccccatagct gagccactgc ctctgatttc aagaacctga 300
 agacgccctc agatcgggtc tcccatttta ttaatcctgg gttcttgtct gggttcaaga 360
 ggatgtcgcg gatgaattcc cataagttag tccctctcgg gttgtgcttt ttgggtgtggc 420
 acttggcagg ggggtcttgc tcccttttca tatcaggtga ctctgcaaca ggaaggtgac 480
 tgggtggtgt catggagatc tgagcccggc agaaagtttt gctgtccaac aaatctactg 540
 tgctaccata gttggtgtca tataaatagt tctngtcttt ccagggtgtc atgatggaag 600
 gctcagtttg ttcagtcttg acaatgacat tgtgtgtgga ctggaacagg tcactactgc 660
 actggccggt ccacttcaga tgctgcaagt tgctgtagag gagntgcccc gccgtccctg 720
 ccgcccgggt gaactcctgc aaactcatgc tgcaaagggt ctgccggttg atgtcgaact 780
 cntggaaagg gatacaattg gcatccagct ggttggtgtc caggaggtga tggagccact 840
 cccacacctg gt 852

<210> 45
 <211> 234
 <212> DNA
 <213> Homo sapien

<400> 45
 acaacagacc ctgtctcgtc aacgacctca tgctcatcaa gttggacgaa tccgtgtccg 60
 agtctgacac catccggagc atcagcattg cttcgcagtg ccctaccgcg gggaactctt 120
 gcctcgtttc tggctggggc ctgctggcga acggcagaat gcctaccgtg ctgcagtgcg 180
 tgaacgtgtc ggtggtgtct gaggaggtct gcagtaagct ctatgaccgc ctgt 234

<210> 46
 <211> 590
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(590)
 <223> n = A,T,C or G

<400> 46
 acttttttatt taaatgttta taaggcagat ctatgagaat gatagaaaac atggtgtgta 60
 atttgatagc aatatttttg agattacaga gtttttagtaa ttaccaatta cacagttaaa 120
 aagaagataa tatattccaa gcanatacaa aatatctaata gaaagatcaa ggcaggaaaa 180
 tgantataac taattgacaa tggaaaatca attttaaatgt gaattgcaca ttatccttta 240
 aaagcttttca aaanaaanaa ttattgcagt ctanttaatt caaacagtgt taaatggtat 300
 caggataaan aactgaaggg canaaagaat taattttcac ttcattgtaac ncacccanat 360
 ttacaatggc ttaaatgcan ggaaaaagca gtggaagtag ggaagtantc aagggtctttc 420
 tggctctctaa tctgccttac tctttgggtg tggctttgat cctctggaga cagctgccag 480
 ggctcctgtt atatccacaa tcccagcagc aagatgaagg gatgaaaaag gacacatgct 540
 gccttccttt gagggagactt catctcactg gccaacactc agtcacatgt 590

<210> 47
 <211> 774
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(774)
 <223> n = A,T,C or G

<400> 47
 acaagggggc ataatgaagg agtgggggana gatttttaaag aaggaaaaaa aacgaggccc 60
 tgaacagaat tttcctgnac aacgggggctt caaaataatt ttcttgggga ggttcaagac 120
 gcttcactgc ttgaaactta aatggatgtg ggacanaatt ttctgtaatg accctgaggg 180
 cattacagac gggactctgg gaggaaggat aaacagaaag gggacaaaag ctaatcccaa 240
 aacatcaaag aaaggaaggt ggcgtcatat cctccagcct acacagttct ccagggtctt 300
 cctcatccct ggaggacgac agtggaggaa caactgacca tgtccccagg ctctgtgtgt 360
 ctggctcctg gtcttcagcc cccagctctg gaagcccacc ctctgctgat cctgcgtggc 420
 ccacactcct tgaacacaca tccccagggtt atattccttg acatggctga acctcctatt 480
 cctacttccg agatgccttg ctccctgcag cctgtcaaaa tcccactcac cctccaaacc 540
 acggcatggg aagcctttct gacttgcttg attactccag catcttgga caatccctga 600
 ttccccactc cttagaggca agatagggtg gttaagagta gggctggacc acttgagacc 660
 aggctgctgg cttcaaattt tggctcattt acgagctatg ggaccttggg caagtnatct 720
 tcacttctat gggcntcatt ttgttctacc tgcaaaatgg gggataataa tagt 774

<210> 48
 <211> 124
 <212> DNA
 <213> Homo sapien

<220>

<221> misc_feature
 <222> (1)...(124)
 <223> n = A,T,C or G

<400> 48
 canaaattga aattttataa aaaggcattt ttctcttata tccataaaat gatataattt 60
 ttgcaantat anaaatgtgt cataaattat aatgttcctt aattacagct caacgcaact 120
 tggt 124

<210> 49
 <211> 147
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(147)
 <223> n = A,T,C or G

<400> 49
 gccgatgcta ctattttatt gcaggaggtg ggggtgtttt tattattctc tcaacagctt 60
 tgtggctaca ggtgggtgtct gactgcatna aaaanttttt tacgggtgat tgcaaaaatt 120
 ttagggcacc catatcccaa gcantgt 147

<210> 50
 <211> 107
 <212> DNA
 <213> Homo sapien

<400> 50
 acattaaatt aataaaaagga ctgttgggggt tctgctaaaa cacatggctt gatatatattgc 60
 atggtttgag gttaggagga gttaggcata tgttttggga gaggggt 107

<210> 51
 <211> 204
 <212> DNA
 <213> Homo sapien

<400> 51
 gtcctaggaa gtctagggga cacacgactc tggggtcacg gggccgacac acttgcacgg 60
 cggaaggaa aggcagagaa gtgacaccgt cagggggaaa tgacagaaag gaaaatcaag 120
 gccttgcaag gtcagaaagg ggactcaggg cttccaccac agccctgccc cacttgcca 180
 cctccctttt gggaccagca atgt 204

<210> 52
 <211> 491
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(491)
 <223> n = A,T,C or G

<400> 52
 acaaagataa catttatctt ataacaaaaa tttgatagtt ttaaaggtta gtatttgtga 60
 ggggtatcttc caaaagacta aagagataac tcaggtaaaa agttagaaat gtataaaaaca 120
 ccatcagaca gggtttttaa aaacaacata ttacaaaatt agacaatcat ccttaaaaaa 180
 aaaacttctt gtatcaattt cttttgttca aaatgactga cttaantatt tttaaatatt 240
 tcanaaacac ttcctcaaaa attttcaana tggtagcttt canatgtnc ctcagtccca 300
 atgttgctca gataaataaa tctcgtgaga acttaccacc caccacaagc tttctggggc 360
 atgcaacagt gtcttttctt tnccttttct tttttttttt ttacaggcac agaaactcat 420
 caattttatt tggataacaa aggggtctcca aattatattg aaaaataaat ccaagttaat 480
 atcactcttg t 491

<210> 53
 <211> 484
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(484)
 <223> n = A,T,C or G

<400> 53
 acataattta gcagggctaa ttaccataag atgctattta ttaanaggtn tatgatctga 60
 gtattaacag ttgctgaagt ttgggtatctt tatgcagcat tttctttttg ctttgataac 120
 actacagaac ccttaaggac actgaaaatt agtaagtaaa gttcagaaac attagctgct 180
 caatcaaatt tctacataac actatagtaa ttaaaacggt aaaaaaaagt gttgaaatct 240
 gcactagtat anaccgctcc tgtcaggata anactgcttt ggaacagaaa gggaaaaanc 300
 agcttttgant ttctttgtgc tgatangagg aaaggctgaa ttaccttggt gcctctccct 360
 aatgattggc aggtcnggta aatnccaaaa catattccaa ctcaacactt cttttccncc 420
 tancttgant ctgtgtattc caggancagg cggatggaat gggccagccc ncggatgttc 480
 cant 484

<210> 54
 <211> 151
 <212> DNA
 <213> Homo sapien

<400> 54
 actaaacctc gtgcttggtga actccataca gaaaacgggtg ccattcctga acacggctgg 60
 ccactgggta tactgctgac aaccgcaaca acaaaaacac aaatccttgg cactggctag 120
 tctatgtcct ctcaagtgcc tttttgtttg t 151

<210> 55
 <211> 91
 <212> DNA
 <213> Homo sapien

<400> 55
 acctggcttg tctccgggtg gttcccggcg cccccacgg tccccagAAC ggacactttc 60
 gccctccagt ggatactcga gccaaagtgg t 91

<210> 56
 <211> 133
 <212> DNA

<212> DNA

<213> Homo sapien

<400> 60

accgtgggtg ccttctacat tcttgacggc tccttcacca acatctgggt ctacttcggc	60
gtcgtgggtc ccttctctt catctcctc cagctgggtg tgctcatcga ctttgcgcac	120
tcctggaacc agcgggtggc gggcaaggcc gaggagtgcg attcccgtgc ctggt	175

<210> 61

<211> 154

<212> DNA

<213> Homo sapien

<400> 61

acccacttt tcctcctgtg agcagtctgg acttctcact gctacatgat gaggggtgagt	60
ggttgttgct cttcaacagt atcctccctt ttccggatct gctgagccgg acagcagtgc	120
tggactgcac agccccgggg ctccacattg ctgt	154

<210> 62

<211> 30

<212> DNA

<213> Homo sapien

<400> 62

cgctcgagcc ctatagttag tcgtattaga	30
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<210> 63

<211> 89

<212> DNA

<213> Homo sapien

<400> 63

acaagtcatt tcagcaccct ttgctcttca aaactgacca tcttttatat ttaatgcttc	60
ctgtatgaat aaaaatggtt atgtcaagt	89

<210> 64

<211> 97

<212> DNA

<213> Homo sapien

<400> 64

accggagtaa ctgagtcggg acgctgaatc tgaatccacc aataaataaa ggttctgcag	60
aatcagtgca tccaggattg gtccttgat ctggggt	97

<210> 65

<211> 377

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(377)

<223> n = A,T,C or G

<400> 65

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acaacaanaa ntcccttctt taggccactg atggaaacct ggaacccctt tttgatggca      60
gcatggcgctc ctaggccttg acacagcggc tgggggtttgg gctntcccaa accgcacacc      120
ccaaccctgg tctaccaca nttctggcta tgggctgtct ctgccactga acatcagggt      180
tcggtcataa natgaaatcc caanggggac agaggtcagt agaggaagct caatgagaaa      240
ggtgctgttt gctcagccag aaaacagctg cctggcattc gccgctgaac tatgaacccg      300
tgggggtgaa ctaccccan gaggaatcat gcctgggcga tgcaanggtg ccaacaggag      360
gggcgggagg agcatgt                                     377

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<210> 66
<211> 305
<212> DNA
<213> Homo sapien

```

```

<400> 66
acgcctttcc ctcagaattc agggaagaga ctgtcgcttg ccttcctccg ttgttgcttg      60
agaacccgtg tgcccttcc caccatatcc accctcgctc catctttgaa ctcaaacacg      120
aggaactaac tgcacctgg tctctcccc agtccccagt tcacctcca tccctcacct      180
tctccactc taagggatat caacactgcc cagcacaggg gccctgaatt tatgtggttt      240
ttatatattt ttaataaga tgcactttat gtcatttttt aataaagtct gaagaattac      300
tgttt                                     305

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<210> 67
<211> 385
<212> DNA
<213> Homo sapien

```

```

<400> 67
actacacaca ctccacttgc ccttgtgaga cactttgtcc cagcacttta ggaatgctga      60
ggtcggacca gccacatctc atgtgcaaga ttgccagca gacatcaggt ctgagagttc      120
cccttttaaa aaaggggact tgcttaaaaa agaagtctag ccacgattgt gtagagcagc      180
tgtgctgtgc tggagattca cttttgagag agttctctc tgagacctga tcttttagagg      240
ctgggcagtc ttgcacatga gatggggctg gtctgatctc agcactcctt agtctgcttg      300
cctctcccag ggccccagcc tggccacacc tgcttacagg gcactctcag atgcccatac      360
catagtttct gtgctagtgg accgt                                     385

```

```

<210> 68
<211> 73
<212> DNA
<213> Homo sapien

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<400> 68
acttaaccag atatattttt accccagatg gggatattct ttgtaaaaaa tgaaaataaa      60
gtttttttaa tgg                                     73

```

```

<210> 69
<211> 536
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(536)
<223> n = A,T,C or G

```

<400> 69
 actagtccag tgtggtggaa ttccattgtg ttgggggctc tcacctcct ctctgcagc 60
 tccagctttg tgctctgcct ctgaggagac catggcccag catctgagta cctgtctgct 120
 cctgtctggcc accctagctg tggccctggc ctggagcccc aaggaggagg ataggataat 180
 cccgggtggc atctataacg cagacctcaa tgatgagtgg gtacagcgtg cccttcactt 240
 cgccatcagc gagtataaca aggccaccaa agatgactac tacagacgtc cgctgcgggt 300
 actaagagcc aggcaacaga ccgttggggg ggtgaattac ttcttcgacg tagaggtggg 360
 ccgaaccata tgtaccaagt cccagcccaa cttggacacc tgtgccttcc atgaacagcc 420
 agaactgcag aagaaacagt tgtgctcttt cgagatctac gaagttccct ggggagaaca 480
 gaangtcctt gggtgaaatc caggtgtcaa gaaatcctan ggatctgttg ccaggc 536

<210> 70
 <211> 477
 <212> DNA
 <213> Homo sapien

<400> 70
 atgacccta acagggggccc tctcagccct cctaattgacc tccggcctag ccatgtgatt 60
 tcacttccac tocataacgc tctcatact aggcctacta accaacacac taaccatata 120
 ccaatgatgg cgcgatgtaa cagcagaaag cacataccaa ggccaccaca caccacctgt 180
 ccaaaaaggc cttcgatacg ggataatcct atttattacc tcagaagttt ttttcttcgc 240
 agggattttt ctgagccttt taccactcca gcctagcccc taccccccta ctaggagggc 300
 actggcccc aacaggcatc accccgctaa atcccctaga agtcccactc ctaaacacat 360
 ccgtattact cgcattcagga gtatcaatca cctgagctca ccatagtcta atagaaaaca 420
 accgaaacca aattattcaa agcactgctt attacaattt tactgggtct ctatttt 477

<210> 71
 <211> 533
 <212> DNA
 <213> Homo sapien
 <220>
 <221> misc_feature
 <222> (1)...(533)
 <223> n = A,T,C or G

<400> 71
 agagctatag gtacagtgtg atctcagctt tgcaaacaca ttttctacat agatagtact 60
 aggtattaat agatatgtaa agaaagaaat cacaccatta ataatggtaa gattgggtta 120
 tgtgatttta gtggtatttt tggcaccctt atatatgttt tccaaacttt cagcagtgat 180
 attatttcca taacttaaaa agtgagtgtt aaaaagaaaa tctccagcaa gcatctcatt 240
 taaataaagg tttgtcatct ttaaaaatac agcaatatgt gactttttta aaaagctgtc 300
 aaataggtgt gaccctacta ataattatta gaaatacatt taaaaacatc gagtacctca 360
 agtcagtttg ccttgaaaaa tatcaaatat aactcttaga gaaatgtaca taaaagaatg 420
 cttcgtaatt ttggagtang aggttccctc ctcaattttg tattttttaa aagtacatgg 480
 taaaaaaaaa aattcacaaac agtatataag gctgtaaaat gaagaattct gcc 533

<210> 72
 <211> 511
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature

<222> (1)...(511)
 <223> n = A,T,C or G

<400> 72
 tattacggaa aaacacacca cataattcaa ctancaaaga anactgcttc agggcgtgta 60
 aaatgaaagg cttccaggca gttatctgat taaagaacac taaaagaggg acaaggctaa 120
 aagccgcagg atgtctacac tatancaggc gctatttggg ttggctggag gagctgtgga 180
 aaacatggan agattggtgc tgganacgc cgtggctatt cctcattgtt attacanagt 240
 gaggttctct gtgtgccac tggtttgaaa accgttctnc aataatgata gaatagtaca 300
 cacatgagaa ctgaaatggc ccaaaccag aaagaaagcc caactagatc ctcagaanac 360
 gcttctaggg acaataaccg atgaagaaaa gatggcctcc ttgtgcccc gtctgttatg 420
 atttctctcc attgcagcna naaaccggtt cttctaagca aacncagggtg atgatggcna 480
 aaatacaccc cctcttgaag naccnggagg a 511

<210> 73
 <211> 499
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(499)
 <223> n = A,T,C or G

<400> 73
 cagtgccagc actggtgcc gtaccagtac caataacagt gccagtgcc gtgccagcac 60
 cagtggaggc ttcagtgtg gtgccagcct gaccgccact ctcacatttg ggctcttcgc 120
 tggccttggg ggagctggg ccagcaccag tggcagctct ggtgcctgtg gtttctccta 180
 caagtgagat tttagatatt gttaatcctg ccagtctttc tcttcaagcc aggggtgcac 240
 ctcagaaacc tactcaacac agcactctag gcagccacta tcaatcaatt gaagttgaca 300
 ctctgcatta aatctatttg ccatctctga aaaaaaaaaa aaaaaaaggg cggccgctcg 360
 antctagagg gcccgtttaa acccgctgat cagcctcgac tgtgccttct anttgccagc 420
 catctgttgt ttgccctcc cccgntgcct tccctgaccc tggaaagtgc cactccact 480
 gtcctttcct aantaaaaat 499

<210> 74
 <211> 537
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(537)
 <223> n = A,T,C or G

<400> 74
 tttcatagga gaacacactg aggagatact tgaagaatth ggattcagcc gcgaagagat 60
 ttatcagctt aactcagata aatcatttga aagtaataag gtaaaagcta gtctcttaact 120
 tccaggccca cggctcaagt gaatttgaat actgcattta cagtgtagag taacacataa 180
 cattgtatgc atggaaacat ggaggaacag tattacagtg tctaccact ctaatcaaga 240
 aaagaattac agactctgat tctacagtga tgattgaatt ctaaaaatgg taatcattag 300
 ggcttttgat ttataanact ttgggtactt atactaaatt atggtagtta tactgccttc 360
 cagtttgctt gatataattg ttgatattaa gattcttgac ttatatattg aatgggttct 420
 actgaaaaan gaatgatata ttcttgaaga catcgatata catttattta cactcttgat 480

tctacaatgt agaaaatgaa ggaaatgccc caaatgttat ggtgataaaa gtcccggt 537

<210> 75
<211> 467
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(467)
<223> n = A,T,C or G

<400> 75
caaanacaat tgttcaaaag atgcaaatga tacactactg ctgcagctca caaacacctc 60
tgcattattac acgtacctcc tctgtctcct caagtagtgt ggtctatattt gccatcatca 120
cctgctgtct gcttagaaga acggctttct gctgcaangg agagaaatca taacagacgg 180
tggcacaagg aggccatctt tctctcatcg gttattgtcc ctagaagcgt cttctgagga 240
tctagtggg ctttctttct gggtttgggc catttcantt ctcatgtgtg tactattcta 300
tcattattgt ataacgggtt tcaaaccngt gggcacncag agaacctcac tctgtaataa 360
caatgaggaa tagccacggg gatctccagc accaaatctc tccatgttnt tccagagctc 420
ctccagccaa cccaaatagc cgctgctatn gtgtagaaca tccctgn 467

<210> 76
<211> 400
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(400)
<223> n = A,T,C or G

<400> 76
aagctgacag cattcgggcc gagatgtctc gctccgtggc cttagctgtg ctgcgctac 60
tctctctttc tggcctggag gctatccagc gtactccaaa gattcagggt tactcacgtc 120
atccagcaga gaatggaaag tcaaatttcc tgaattgcta tgtgtctggg tttcatccat 180
ccgacattga agttgactta ctgaagaatg gagagagaat tgaaaaagt gagcattcag 240
acttgtcttt cagcaaggac tggctttct atctcttgta ctacactgaa ttcaccccca 300
ctgaaaaaga tgagtatgcc tgccgtgtga accatgtgac tttgtcacag cccaagatng 360
ttnagtggga tcganacatg taagcagcan catgggaggt 400

<210> 77
<211> 248
<212> DNA
<213> Homo sapien

<400> 77
ctggagtgcc ttggtgtttc aagccccctgc aggaagcaga atgcacctc tgaggcacct 60
ccagctgccc cggcggggga tgcgaggctc ggagcaccct tgccgggctg tgattgctgc 120
caggcactgt tcatctcagc ttttctgtcc ctttgcctcc ggcaagcgt tctgctgaaa 180
gttcatatct ggagcctgat gtcttaacga ataaaggctc catgctccac ccgaaaaaaa 240
aaaaaaaaa 248

<210> 78

<211> 201
 <212> DNA
 <213> Homo sapien

<400> 78
 actagtccag tgtggtggaa ttccattgtg ttgggcccac cacaatggct acctttaaca 60
 tcaccagac cccgccctgc cccgtgcccc cgctgctgct aacgacagta tgatgcttac 120
 tctgtactc ggaaactatt tttatgtaat taatgtatgc tttcttgctt ataaatgcct 180
 gatttaaaaa aaaaaaaaaa a 201

<210> 79
 <211> 552
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(552)
 <223> n = A,T,C or G

<400> 79
 tccttttgtt aggtttttga gacaacccta gacctaaact gtgtcacaga cttctgaatg 60
 tttaggcagt gctagtaatt tcctcgtaat gattctgtta ttactttcct attctttatt 120
 cctctttcct ctgaagatta atgaagttga aaattgaggt ggataaatac aaaaaggtag 180
 tgtgatagta taagtatcta agtgcagatg aaagtgtgtt atatatatcc attcaaaatt 240
 atgcaagtta gtaattactc aggggttaact aaattacttt aatatgctgt tgaacctact 300
 ctgttccttg gctagaaaaa attataaaca ggactttgtt agtttgggaa gccaaattga 360
 taatattcta tgttctaaaa gttgggctat acataaanta tnaagaaata tggaatttta 420
 ttcccaggaa tatgggggtt atttatgaat antaccggg anagaagttt tgantnaaac 480
 cngtttttgt taatacgtta atatgtcctn aatnaacaag gcntgactta tttccaaaaa 540
 aaaaaaaaaa aa 552

<210> 80
 <211> 476
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(476)
 <223> n = A,T,C or G

<400> 80
 acagggattt gagatgctaa ggccccagag atcgtttgat ccaaccctct tattttcaga 60
 ggggaaaatg gggcctagaa gttacagagc atctagctgg tgcgctggca cccctggcct 120
 cacacagact cccgagtagc tgggactaca ggcacacagt cactgaagca ggccctgttt 180
 gcaattcacg ttgccacctc caacttaaac attcttcata tgtgatgtcc ttagtcacta 240
 aggttaaaact ttcccaccca gaaaaggcaa cttagataaa atcttagagt actttcatal 300
 tcttctaagt cctcttcag cctcactttg agtcctcctt gggggttgat aggaantntc 360
 tcttggtttt ctcaataaaa tctctatcca tctcatgttt aatttggtac gcntaaaaat 420
 gctgaaaaaa ttaaaatgtt ctggtttcnc tttaaaaaaa aaaaaaaaaa aaaaaa 476

<210> 81
 <211> 232

<212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(232)
 <223> n = A,T,C or G

<400> 81
 tttttttttg tatgcentcn ctgtggngtt attgttgctg ccaccctgga ggagcccagt 60
 ttctttctgta tctttctttt ctgggggata ttcttggtc tgccctcca ttcccagcct 120
 ctcaccccca tcttgcaactt ttgctagggg tggaggcgct ttcttggtag cccctcagag 180
 actcagtcag cggaataag tcttaggggt ggggggtgtg gcaagccggc ct 232

<210> 82
 <211> 383
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(383)
 <223> n = A,T,C or G

<400> 82
 aggcgggagc agaagctaaa gccaaagccc aagaagagtg gcagtgccag cactgggtgcc 60
 agtaccagta ccaataacat gccagtgccg gtgccagcac cagtgggtggc ttccagtctg 120
 gtgccagcct gaccgccact ctcacatttg ggctcttcgc tggccttggg ggagctgggt 180
 ccagcaccag tggcagctct ggtgcctgtg gtttctccta caagtgaat tttagatatt 240
 gttaatcctg ccagtctttc tcttcaagcc aggggtgcac ctcagaaacc tactcaacac 300
 agcactctng gcagccacta tcaatcaatt gaagttgaca ctctgcatta aatctatttg 360
 ccatttcaaa aaaaaaaaaa aaa 383

<210> 83
 <211> 494
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(494)
 <223> n = A,T,C or G

<400> 83
 accgaattgg gaccgctggc ttataagcga tcatgtcttc cagtattacc tcaacgagca 60
 gggagatcga gtctatacgc tgaagaaatt tgaccgatg ggacaacaga cctgctcagc 120
 ccatcctgct cggttctccc cagatgacaa atactctcga caccgaatca ccatcaagaa 180
 acgcttcaag gtgctcatga ccagcaacc gcgccctgtc ctctgagggg ccttaaactg 240
 atgtcttttc tgccacctgt taccctcgg agactccgta accaaactct tcggactgtg 300
 agccctgatg cttttttgcc agccatactc tttggcntcc agtctctcgt ggcgattgat 360
 tatgcttgtg tgaggcaatc atgggtggcat caccatnaa gggaacacat ttganttttt 420
 tttcncatat tttaaattac naccagaata ntccagaata aatgaattga aaaactctta 480
 aaaaaaaaaa aaaa 494

<210> 84
 <211> 380
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(380)
 <223> n = A,T,C or G

<400> 84
 gctggtagcc tatggcgtgg ccacggangg gtcctgagg cacgggacag tgacttccca 60
 agtatcctgc gccgcgtctt ctaccgtccc tacctgcaga tcttcgggca gattccccag 120
 gaggacatgg acgtggccct catggagcac agcaactgct cgtcggagcc cggcttcttg 180
 gcacaccctc ctggggccca ggccggcacc tgcgtctccc agtatgcca ctggctggtg 240
 gtgctgtccc tcgtcatctt cctgctcgtg gccaacatcc tgctggtcac ttgctcattg 300
 ccatgttcag ttacacattc ggcaaagtac agggcaacag cnatctctac tgggaaggcc 360
 agcgttnccg cctcatccgg 380

<210> 85
 <211> 481
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(481)
 <223> n = A,T,C or G

<400> 85
 gagttagctc ctccacaacc ttgatgaggt cgtctgcagt ggccctctcgc ttcataccgc 60
 tnccatcgtc atactgtagg tttgccacca cctcctgcat cttggggcgg ctaatatcca 120
 ggaaactctc aatcaagtca ccgtcnatna aacctgtggc tggttctgtc ttccgctcgg 180
 tgtgaaagga tctccagaag gagtgctcga tcttccccac acttttgatg actttattga 240
 gtcgattctg catgtccagc aggaggttgt accagctctc tgacagtgag gtcaccagcc 300
 ctatcatgcc nttgaacgtg ccgaagaaca ccgagccttg tgtggggggg gnagtctcac 360
 ccagattctg cattaccaga nagccgtggc aaaaganatt gacaactcgc ccaggngaa 420
 aaagaacacc tcctggaagt gctngccgct cctcgctcent tgggtggngc gcntnccttt 480
 t 481

<210> 86
 <211> 472
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(472)
 <223> n = A,T,C or G

<400> 86
 aacatcttcc tgtataatgc tgtgtaatat cgatccgatn ttgtctgctg agaattcatt 60
 acttggaaaa gcaacttnaa gcctggacac tgggtattaaa attcacaata tgcaacactt 120
 taaacagtgt gtcaatctgc tcccttactt tgtcatcacc agtctgggaa taagggtatg 180


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ccctattcac acctgttaaa agggcgctaa gcatttttga ttcaacatct ttttttttga 240
cacaagtcgc aaaaaagcaa aagtaaacag ttnttaattt gttagccaat tcacttttctt 300
catgggacag agccatttga tttaaaaagc aaattgcata atattgagct ttgggagctg 360
atatntgagc ggaagantag cttttctact tcaccagaca caactccttt catattggga 420
tgttnacnaa agttatgtct cttacagatg ggatgctttt gtggcaattc tg 472

```

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<210> 87
<211> 413
<212> DNA
<213> Homo sapien

```

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<220>
<221> misc_feature
<222> (1)...(413)
<223> n = A,T,C or G

```

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<400> 87
agaaaccagt atctctnaaa acaacctctc ataccttgtg gacctaatct tgtgtgcgtg 60
tgtgtgtgcg cgcataattat atagacaggc acatcttttt tacttttcta aaagcttatg 120
cctcttttgg atctatatct gtgaaagttt taatgatctg ccataatgtc ttggggacct 180
ttgtcttctg tgtaaatggg actagagaaa acacctatnt tatgagtcaa tctagttngt 240
tttattcgac atgaaggaaa tttccagatn acaacactna caaactctcc cttgactagg 300
ggggacaaaag aaaagcnaaa ctgaacatna gaaacaattn cctgggtgaga aattncataa 360
acagaaattg ggtngtatat tgaaanannn catcattnaa acgttttttt ttt 413

```

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<210> 88
<211> 448
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(448)
<223> n = A,T,C or G

```

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<400> 88
cgcagcgggt cctctctatc tagctccagc ctctcgcttg ccccaactccc cgcgtcccgc 60
gtcctagccn accatggccg ggcccctgcg cgcctcgctg ctctctgctg ccactcctggc 120
cgtggccctg gccgtgagcc ccgcggcccg ctccagtcct ggcaagccgc cgcgcctggg 180
gggaggccca tggaccccg cgtggaagaag aaggtgtgcg gcgtgcactg gactttgccc 240
tcggcnanta caacaaaccc gcaacnactt ttaccnagcn cgcgctgcag gttgtgccgc 300
cccaancaaa ttgttactng gggttaantaa ttcttggaag ttgaacctgg gccaaacnng 360
tttaccagaa ccnagccaat tngaacaatt nccccctcat aacagcccct tttaaaaagg 420
gaancantcc tgntcttttc caaatctt

```

```

<210> 89
<211> 463
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(463)
<223> n = A,T,C or G

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```

<400> 89
gaattttgtg cactggccac tgtgatggaa ccattgggcc aggatgcttt gagtttatca      60
gtagtgattc tgccaaagtt ggtggtgtaa catgagtatg taaaatgtca aaaaattagc      120
agagggtctag gtctgcatat cagcagacag tttgtccgtg tattttgtag ccttgaagtt      180
ctcagtgaca agttnnttct gatgcgaagt tctnattcca gtgttttagt cctttgcatc      240
tttnatgtn agacttgccct ctntnaaatt gcttttgtnt tctgcaggta ctatctgtgg      300
tttaacaaaa tagaannact tctctgcttn gaanatttga atatcttaca tctnaaaatn      360
aattctctcc ccatannaaa acccangccc ttggganaat ttgaaaaang gntccttcnn      420
aattcnnana anttcagntn tcatacaaca naacngganc ccc                        463

```

```

<210> 90
<211> 400
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(400)
<223> n = A,T,C or G

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<400> 90
agggattgaa ggtctnttnt actgtcggac tgttcancca ccaactctac aagttgctgt      60
cttccactca ctgtctgtaa gentnttaac ccagactgta tcttcataaa tagaacaaat      120
tcttcaccag tcacatcttc taggaccttt ttggattcag ttagtataag ctcttccact      180
tcctttgtta agacttcac tcggtaaagtc ttaagttttg tagaaaaggaa ttaattgct      240
cgttctctaa caatgtcctc tccttgaagt atttggttga acaaccacc tnaagtccct      300
ttgtgcatcc attttaaata tacttaatag ggcattggtn cactagggtta aattctgcaa      360
gagtcactctg tctgcaaaaag ttgcgttagt atatctgcca                        400

```

```

<210> 91
<211> 480
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(480)
<223> n = A,T,C or G

```

```

<400> 91
gagctcggat ccaataatct ttgtctgagg gcagcacaca tatncagtgc catggnaact      60
ggtctacccc acatgggagc agcatgccgt agntatataa ggtcattccc tgagtcagac      120
atgctctttt gactaccgtg tgccagtgtc ggtgattctc acacacctcc nncgctctt      180
tgtggaaaaa ctggcacttg nctggaacta gcaagacatc acttacaaat tcaccacga      240
gacacttgaa aggtgtaaca aagcgactct tgcattgctt tttgtccctc cggcaccagt      300
tgtcaatact aaccgcgtgg tttgcctcca tcacatttgt gatctgtagc tctggataca      360
tctcctgaca gtactgaaga acttcttctt ttgtttcaaa agcaactctt ggtgcctgtt      420
ngatcagggtt cccatttccc agtccgaatg ttcacatggc atatnttact tcccacaaaa      480

```

```

<210> 92
<211> 477
<212> DNA
<213> Homo sapien

```

<220>
 <221> misc_feature
 <222> (1)...(477)
 <223> n = A,T,C or G

<400> 92
 atacagccca natcccacca cgaagatgcg cttgttgact gagaacctga tgcggtcact 60
 ggtcccgtg tagccccagc gactctccac ctgctggaag cggttgatgc tgcactcctt 120
 cccacgcagg cagcagcggg gccggccaat gaactccact cgtggccttg ggttgacggt 180
 taantgcagg aagaggctga ccacctcgcg gtccaccagg atgcccgact gtgcgggacc 240
 tgcagcgaaa ctctcgatg gtcattgagc ggaagcgaat gangcccagg gccttgccca 300
 gaaccttccg cctgttctct ggcgctacct gcagctgctg ccgctnacac tcggcctcgg 360
 accagcggac aaacggcggt gaacagccgc acctcacgga tgcccantgt gtcgcgctcc 420
 aggaacggcn ccagcgtgtc cagggtcaatg tcggtgaanc ctccgcgggt aatggcg 477

<210> 93
 <211> 377
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(377)
 <223> n = A,T,C or G

<400> 93
 gaacggctgg accttgccctc gcattgtgct gctggcagga ataccttggc aagcagctcc 60
 agtccgagca gcccagacc gctgccgccc gaagctaagc ctgcctctgg ccttcccctc 120
 cgcctcaatg cagaaccant agtgggagca ctgtgttttag agttaagagt gaacactgtn 180
 tgattttact tgggaatttc ctctgttata tagcttttcc caatgctaata tccaaacaa 240
 caacaacaaa ataacatgtt tgctgttna gttgtataaa agtangtgat tctgtatnta 300
 aagaaaatat tactgttaca tatactgctt gcaantctctg tatttattgg tncctctggaa 360
 ataaatatat tattaata 377

<210> 94
 <211> 495
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(495)
 <223> n = A,T,C or G

<400> 94
 ccctttgagg ggttagggctc cagttcccag tggaagaaac aggccaggag aantgcgtgc 60
 cgagctgang cagatttccc acagtgaccc cagagccctg ggctatagtc tctgacctt 120
 ccaaggaaa accaccttct ggggacatgg gctggagggc aggacctaga ggcaccaagg 180
 gaaggcccca ttccggggct gttccccgag gaggaaggga aggggctctg tgtgcccccc 240
 acgaggaana ggccctgant cctgggatca nacacccctt cagtggtatc cccacacaaa 300
 tgcaagctca ccaaggtccc ctctcagtc cttccctaca cctgaacgg ncactggccc 360
 acaccacccc agancancca cccgccatgg ggaatgtnt caaggaatcg cngggcaacg 420
 tggactctng tcccnnaagg gggcagaatc tccaatagan gganngaacc cttgctnana 480

aaaaaaaaana aaaaa

495

<210> 95
<211> 472
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(472)
<223> n = A,T,C or G

<400> 95
ggttacttgg tttcattgcc accacttagt ggatgtcatt tagaaccatt ttgtctgctc 60
cctctggaag ccttgcgcag agcggacttt gtaattggtg gagaataact gctgaatttt 120
tagctgtttt gagttgattc gcaccactgc accacaactc aatatgaaaa ctatttnact 180
tatttattat cttgtgaaaa gtatacaatg aaaattttgt tcatactgta tttatcaagt 240
atgatgaaaa gcaatagata tatattcttt tattatgtnn aattatgatt gccattatta 300
atcggcaaaa tgtggagtgt atgttctttt cacagtaata tatgcctttt gtaacttcac 360
ttgggtattt tattgtaaat gaattacaaa attcttaatt taagaaaatg gtangttata 420
tttanttcan taatttcttt ccttggtttac gttaattttg aaaagaatgc at 472

<210> 96
<211> 476
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(476)
<223> n = A,T,C or G

<400> 96
ctgaagcatt tcttcaaact tntctacttt tgtcattgat acctgtagta agttgacaat 60
gtggtgaaat ttcaaaatta tatgtaactt ctactagttt tactttctcc cccaagtctt 120
ttttaactca tgattttttac acacacaatc cagaacttat tatatagcct ctaagtcttt 180
attcttcaca gtagatgatg aaagagtcct ccagtgtctt gngcanaatg ttctagntat 240
agctggatac atacngtggg agttctataa actcatacct cagtgggact naaccaaaat 300
tgtgttagtc tcaattccta ccacactgag ggagcctccc aaatcactat attcttatct 360
gcaggctactc ctccagaaaa acngacaggg caggcttgca tgaaaaagtn acatctgcgt 420
tacaaagtct atcttctcta nangtctgtn aaggaacaat ttaatcttct agcttt 476

<210> 97
<211> 479
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(479)
<223> n = A,T,C or G

<400> 97
actctttcta atgctgatat gatcttgagt ataagaatgc atatgtcact agaattggata 60

aaataatgct	gcaaacttaa	tgttcttatg	caaaatggaa	cgctaataa	acacagctta	120
caatcgcaaa	tcaaaactca	caagtgtctca	tctgtttag	athtagtgta	ataagactta	180
gattgtgctc	cttcggatat	gattgtttct	canatcttg	gcaatnttcc	ttagtcaa	240
caggctacta	gaattctgtt	attggatatn	tgagagcatg	aaatttttaa	naatacactt	300
gtgattatna	aattaatcac	aaatttcaact	tatacctgct	atcagcagct	agaaaaacat	360
ntnnnttttta	natcaaagta	ttttgtgttt	ggaantgttn	aaatgaaatc	tgaatgtggg	420
ttcnatctta	ttttttcccn	gacnactant	tnctttttta	gggnctattc	tgancctatc	479

<210> 98

<211> 461

<212> DNA

<213> Homo sapien

<400> 98

agtgacttgt	cctccaacaa	aacccttga	tcaagtttgt	ggcactgaca	atcagaccta	60
tgctagtcc	tgctactat	tcgtactaa	atgcagactg	gaggggacca	aaaaggggca	120
tcaactccag	ctggattatt	ttggagcctg	caaactctatt	cctacttgta	cggactttga	180
agtgattcag	tttctctac	ggatgagaga	ctggctcaag	aatatcctca	tcagacttta	240
tgaagccact	ctgaacacgc	tggttatcta	gatgagaaca	gagaaataaa	gtcagaaaat	300
ttacctggag	aaaagaggct	ttggctgggg	accatcccat	tgaaccttct	cttaaggact	360
ttaagaaaaa	ctaccacatg	ttgtgtatcc	tggtgcgggc	cgtttatgaa	ctgaccaccc	420
tttgaataa	tcttgacgct	cctgaacttg	ctcctctgcg	a		461

<210> 99

<211> 171

<212> DNA

<213> Homo sapien

<400> 99

gtggcgcgc	gcaggtgttt	cctcgtagcg	cagggccccc	tcccttcccc	aggcgtccct	60
cggcgcctct	gcgggcccga	ggaggagcgg	ctggcggtg	gggggagtgt	gaccacccct	120
cggtgagaaa	agccttctct	agcgatctga	gaggcgtgcc	ttgggggtac	c	171

<210> 100

<211> 269

<212> DNA

<213> Homo sapien

<400> 100

cggcgcgaag	tgcaactcca	gctggggccg	tgcgagcga	gattctgcca	gcagttggtc	60
cgactgagac	gacggcgggc	gcgacagtcg	caggtgcagc	gcgggcgcct	ggggtcttgc	120
aaggctgagc	tgacgccgca	gaggtcgtgt	cacgtccac	gaccttgacg	cogtcgggga	180
cagccggaac	agagcccggg	gaagcgggag	gcctcgggga	gcccctcggg	aagggcggcc	240
cgagagatac	gcaggtgcag	gtggccgcc				269

<210> 101

<211> 405

<212> DNA

<213> Homo sapien

<400> 101

tttttttttt	ttttggaatc	tactgagcgc	acagcaggtc	agcaacaagt	ttattttgca	60
gctagcaagg	taacagggtg	gggcatgggt	acatgttcag	gtcaacttcc	tttgctgtgg	120
ttgattgggt	tgtctttatg	ggggcggggt	ggggtagggg	aaacgaagca	aataacatgg	180

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agtgggtgca ccctccctgt agaacctggt tacaaagctt ggggcagttc acctggctctg 240
tgaccgtcat ttctcttgaca tcaatgttat tagaagtcag gatatctttt agagagtcca 300
ctgttctgga gggagattag ggtttcttgc caaatccaac aaaatccact gaaaaagttg 360
gatgatcagt acgaataccg aggcattatc tcatatcggt ggcca 405

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```

<210> 102
<211> 470
<212> DNA
<213> Homo sapien

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```

<400> 102
tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 60
ggcacttaat ccattttttat ttcaaaatgt ctacaaattt aatcccatta tacgggtattt 120
tcaaaatcta aattattcaa attagccaaa tccttaccaa ataataccca aaaatcaaaa 180
atatacttct ttcagcaaac ttgttacata aattaaaaaa atatatacgg ctgggtgtttt 240
caaagtacaa ttatcttaac actgcaaaca ttttaaggaa ctaaaataaa aaaaaacact 300
ccgcaaaggt taaaggggaa aacaaattct tttaacaacac cattataaaa atcatatctc 360
aaatcttagg ggaatatata cttcacacgg gatcttaact ttactcact ttgtttattt 420
ttttaaacca ttgtttgggc ccaacacaat ggaatcccc ctggactagt 470

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```

<210> 103
<211> 581
<212> DNA
<213> Homo sapien

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```

<400> 103
tttttttttt ttttttttga ccccccctctt ataaaaaaca agttaccatt ttatttttact 60
tacacatatt tatttttataa ttgggtattag atattcaaaa ggcagctttt aaaatcaaac 120
taaatggaaa ctgccttaga tacataatct ttaggaatta gcttaaaatc tgccataagt 180
gaaaatcttc tctagctctt ttgactgtaa atttttgact cttgtaaaac atccaaattc 240
atttttcttg tctttaaaat tatctaattc ttccattttt tccttattcc aagtcaattt 300
gcttctctag cctcatttcc tagctcttat ctactattag taagtggctt ttttcctaaa 360
agggaaaaca ggaagagaaa tggcacacaa aacaaacatt ttatattcat atttctacct 420
acgttaataa aatagcattt tgtgaagcca gctcaaaaga aggcttagat ccttttatgt 480
ccatttttagt cactaaacga tatcaaagtg ccagaatgca aaagggttgt gaacatttat 540
tcaaaagcta atataagata tttcacatac tcatctttct g 581

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```

<210> 104
<211> 578
<212> DNA
<213> Homo sapien

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```

<400> 104
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cactctctag atagggcag aagaaaactc atctttccag ctttaaaata acaatcaaat 120
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 ggcgagaaat gaggaagaaa agaaaaggat tacgcatact gttctttcta tggaaggatt 480
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<210> 108
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<212> PRT
<213> Homo sapien

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35 40 45
Gly Lys Arg Ser Leu Val Leu Asp Leu Lys Gln Pro Arg Gly Ala Ala
50 55 60
Val Leu Arg Arg Leu Cys Lys Arg Ser Asp Val Leu Leu Glu Pro Phe
65 70 75 80
Arg Arg Gly Val Met Glu Lys Leu Gln Leu Gly Pro Glu Ile Leu Gln
85 90 95
Arg Glu Asn Pro Arg Leu Ile Tyr Ala Arg Leu Ser Gly Phe Gly Gln
100 105 110
Ser Gly Ser Phe Cys Arg Leu Ala Gly His Asp Ile Asn Tyr Leu Ala
115 120 125
Leu Ser Gly Val Leu Ser Lys Ile Gly Arg Ser Gly Glu Asn Pro Tyr
130 135 140
Ala Pro Leu Asn Leu Leu Ala Asp Phe Ala Gly Gly Gly Leu Met Cys
145 150 155 160
Ala Leu Gly Ile Ile Met Ala Leu Phe Asp Arg Thr Arg Thr Asp Lys
165 170 175
Gly Gln Val Ile Asp Ala Asn Met Val Glu Gly Thr Ala Tyr Leu Ser
180 185 190
Ser Phe Leu Trp Lys Thr Gln Lys Ser Ser Leu Trp Glu Ala Pro Arg
195 200 205
Gly Gln Asn Met Leu Asp Gly Gly Ala Pro Phe Tyr Thr Thr Tyr Arg
210 215 220
Thr Ala Asp Gly Glu Phe Met Ala Val Gly Ala Ile Glu Pro Gln Phe
225 230 235 240
Tyr Glu Leu Leu Ile Lys Gly Leu Gly Leu Lys Ser Asp Glu Leu Pro
245 250 255
Asn Gln Met Ser Met Asp Asp Trp Pro Glu Met Lys Lys Lys Phe Ala
260 265 270
Asp Val Phe Ala Lys Lys Thr Lys Ala Glu Trp Cys Gln Ile Phe Asp
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005136.03390

Gly Thr Asp Ala Cys Val Thr Pro Val Leu Thr Phe Glu Glu Val Val
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<210> 109
 <211> 1524
 <212> DNA
 <213> Homo sapien

<400> 109

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 <212> DNA
 <213> Homo sapien

<400> 110

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3410

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<213> Homo sapien

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<211> 315
<212> PRT
<213> Homo sapien

<400> 112
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Phe Phe Leu Phe Phe Leu Gly Val Trp Leu Val Ala Tyr Gly Val Ala
35 40 45
Thr Glu Gly Leu Leu Arg Pro Arg Asp Ser Asp Phe Pro Ser Ile Leu
50 55 60
Arg Arg Val Phe Tyr Arg Pro Tyr Leu Gln Ile Phe Gly Gln Ile Pro
65 70 75 80
Gln Glu Asp Met Asp Val Ala Leu Met Glu His Ser Asn Cys Ser Ser
85 90 95
Glu Pro Gly Phe Trp Ala His Pro Pro Gly Ala Gln Ala Gly Thr Cys
100 105 110
Val Ser Gln Tyr Ala Asn Trp Leu Val Val Leu Leu Leu Val Ile Phe
115 120 125
Leu Leu Val Ala Asn Ile Leu Leu Val Asn Leu Leu Ile Ala Met Phe

006230"925950

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Ala Pro Pro Phe Ile Val Ile Ser His Leu Arg Leu Leu Leu Arg Gln
      180              185              190
Leu Cys Arg Arg Pro Arg Ser Pro Gln Pro Ser Ser Pro Ala Leu Glu
      195              200              205
His Phe Arg Val Tyr Leu Ser Lys Glu Ala Glu Arg Lys Leu Leu Thr
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Trp Glu Ser Val His Lys Glu Asn Phe Leu Leu Ala Arg Ala Arg Asp
225              230              235              240
Lys Arg Glu Ser Asp Ser Glu Arg Leu Lys Arg Thr Ser Gln Lys Val
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Asp Leu Ala Leu Lys Gln Leu Gly His Ile Arg Glu Tyr Glu Gln Arg
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Leu Lys Val Leu Glu Arg Glu Val Gln Gln Cys Ser Arg Val Leu Gly
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<210> 113

<211> 553

<212> PRT

<213> Homo sapien

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Glu Glu Lys Phe Met Thr Met Val Leu Gly Ile Gly Pro Val Leu Gly
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Arg Tyr Gly Arg Arg Arg Pro Phe Ile Trp Ala Leu Ser Leu Gly Ile
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Val Gly Leu Leu Asp Phe Cys Gly Gln Val Cys Phe Thr Pro Leu Glu
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Ala Leu Leu Ser Asp Leu Phe Arg Asp Pro Asp His Cys Arg Gln Ala
145              150              155              160
Tyr Ser Val Tyr Ala Phe Met Ile Ser Leu Gly Gly Cys Leu Gly Tyr
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Leu Leu Pro Ala Ile Asp Trp Asp Thr Ser Ala Leu Ala Pro Tyr Leu
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 Pro Thr Glu Pro Ala Glu Gly Leu Ser Ala Pro Ser Leu Ser Pro His
 225 230 235 240
 Cys Cys Pro Cys Arg Ala Arg Leu Ala Phe Arg Asn Leu Gly Ala Leu
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 Val Arg Met Gly Ser Leu Gly Leu Phe Leu Gln Cys Ala Ile Ser Leu
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 Ala Val Tyr Leu Ala Ser Val Ala Ala Phe Pro Val Ala Ala Gly Ala
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 Ser Leu Tyr His Arg Glu Lys Gln Val Phe Leu Pro Lys Tyr Arg Gly
 405 410 415
 Asp Thr Gly Gly Ala Ser Ser Glu Asp Ser Leu Met Thr Ser Phe Leu
 420 425 430
 Pro Gly Pro Lys Pro Gly Ala Pro Phe Pro Asn Gly His Val Gly Ala
 435 440 445
 Gly Gly Ser Gly Leu Leu Pro Pro Pro Pro Ala Leu Cys Gly Ala Ser
 450 455 460
 Ala Cys Asp Val Ser Val Arg Val Val Val Gly Glu Pro Thr Glu Ala
 465 470 475 480
 Arg Val Val Pro Gly Arg Gly Ile Cys Leu Asp Leu Ala Ile Leu Asp
 485 490 495
 Ser Ala Phe Leu Leu Ser Gln Val Ala Pro Ser Leu Phe Met Gly Ser
 500 505 510
 Ile Val Gln Leu Ser Gln Ser Val Thr Ala Tyr Met Val Ser Ala Ala
 515 520 525
 Gly Leu Gly Leu Val Ala Ile Tyr Phe Ala Thr Gln Val Val Phe Asp
 530 535 540
 Lys Ser Asp Leu Ala Lys Tyr Ser Ala
 545 550

<210> 114

<211> 241

<212> PRT

<213> Homo sapien

<400> 114

Met Gln Cys Phe Ser Phe Ile Lys Thr Met Met Ile Leu Phe Asn Leu

006230" 032590

1 5 10 15
 Leu Ile Phe Leu Cys Gly Ala Ala Leu Leu Ala Val Gly Ile Trp Val
 20 25 30
 Ser Ile Asp Gly Ala Ser Phe Leu Lys Ile Phe Gly Pro Leu Ser Ser
 35 40 45
 Ser Ala Met Gln Phe Val Asn Val Gly Tyr Phe Leu Ile Ala Ala Gly
 50 55 60
 Val Val Val Phe Ala Leu Gly Phe Leu Gly Cys Tyr Gly Ala Lys Thr
 65 70 75 80
 Glu Ser Lys Cys Ala Leu Val Thr Phe Phe Ile Leu Leu Leu Ile
 85 90 95
 Phe Ile Ala Glu Val Ala Ala Ala Val Val Ala Leu Val Tyr Thr Thr
 100 105 110
 Met Ala Glu His Phe Leu Thr Leu Leu Val Val Pro Ala Ile Lys Lys
 115 120 125
 Asp Tyr Gly Ser Gln Glu Asp Phe Thr Gln Val Trp Asn Thr Thr Met
 130 135 140
 Lys Gly Leu Lys Cys Cys Gly Phe Thr Asn Tyr Thr Asp Phe Glu Asp
 145 150 155 160
 Ser Pro Tyr Phe Lys Glu Asn Ser Ala Phe Pro Pro Phe Cys Cys Asn
 165 170 175
 Asp Asn Val Thr Asn Thr Ala Asn Glu Thr Cys Thr Lys Gln Lys Ala
 180 185 190
 His Asp Gln Lys Val Glu Gly Cys Phe Asn Gln Leu Leu Tyr Asp Ile
 195 200 205
 Arg Thr Asn Ala Val Thr Val Gly Gly Val Ala Ala Gly Ile Gly Gly
 210 215 220
 Leu Glu Leu Ala Ala Met Ile Val Ser Met Tyr Leu Tyr Cys Asn Leu
 225 230 235 240
 Gln

<210> 115
 <211> 366
 <212> DNA
 <213> Homo sapien

<400> 115
 gctctttctc tcccctcctc tgaatttaaat tctttcaact tgcaatttgc aaggattaca 60
 catttcactg tgatgtatat tgtgttgcaa aaaaaaaaaa gtgtctttgt ttaaaattac 120
 ttggtttgtg aatccatctt gctttttccc cattggaact agtcattaac ccatctctga 180
 actggtagaa aaacatctga agagctagtc tatcagcatc tgacaggtga attggatggg 240
 tctcagaacc atttcaccca gacagcctgt ttctatcctg ttttaataaat tagtttgggt 300
 tctctacatg cataacaaac cctgctccaa tctgtcacat aaaagtctgt gacttgaagt 360
 ttagtc 366

<210> 116
 <211> 282
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(282)

006280" 9225960

agtaagctgg cccttctaataaaaagaaaat tgaaagggtt ctcactaanc ggaattaant 180
aatggantca aganactccc aggccctcagc gt 212

<210> 120
<211> 90
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(90)
<223> n = A,T,C or G

<400> 120
actcgttgca natcaggggc cccccagagt caccggttgca ggagtccttc tggctcttgcc 60
ctccgccggc gcagaacatg ctgggggtggt 90

<210> 121
<211> 218
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(218)
<223> n = A,T,C or G

<400> 121
tgtancgtga anacgacaga naggggttgtc aaaaatggag aanccttgaa gtcattttga 60
gaataagatt tgctaaaaga tttgggggcta aaacatgggtt attgggagac atttctgaag 120
atatncangt aaattangga atgaattcat gggttcttttg ggaattcctt tacgatngcc 180
agcatanact tcatgtgggg atancagcta cccttgta 218

<210> 122
<211> 171
<212> DNA
<213> Homo sapien

<400> 122
taggggtgta tgcaactgta aggacaaaaa ttgagactca actggcttaa ccaataaagg 60
catttgtag ctcattggaac aggaagtcgg atgggtggggc atcttcagtg ctgcatgagt 120
caccaccccg gcgggggtcat ctgtgccaca ggtccctgtt gacagtgcgg t 171

<210> 123
<211> 76
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(76)
<223> n = A,T,C or G

<400> 123

tgtagcgtga agacnacaga atgggtgtgtg ctgtgctatc caggaacaca tttattatca 60
ttatcaanta ttgtgt 76

<210> 124
<211> 131
<212> DNA
<213> Homo sapien

<400> 124
acctttcccc aaggccaatg tcctgtgtgc taactggccg gctgcaggac agctgcaatt 60
caatgtgctg ggtcatatgg aggggaggag actctaaaat agccaatttt attctcttgg 120
ttaagatttg t 131

<210> 125
<211> 432
<212> DNA
<213> Homo sapien

<400> 125
actttatcta ctggctatga aatagatggg ggaaaattgc gttaccaact ataccactgg 60
cttgaaaaag aggtgatagc tcttcagagg acttgtgact ttgctcaga tgctgaagaa 120
ctacagtctg catttggcag aaatgaagat gaatttggat taaatgagga tgctgaagat 180
ttgcctcacc aaacaaaagt gaaacaactg agagaaaatt ttcaggaaaa aagacagtgg 240
ctcttgaagt atcagtcact tttgagaatg tttcttagtt actgcatact tcatggatcc 300
catggtgggg gtcttgcac tgtaagaatg gaattgattt tgcttttgca agaatctcag 360
caggaaacat cagaaccact attttctagc cctctgtcag agcaaaccctc agtgcctctc 420
ctctttgctt gt 432

<210> 126
<211> 112
<212> DNA
<213> Homo sapien

<400> 126
acacaacttg aatagtaaaa tagaaactga gctgaaattt ctaattcact ttctaaccat 60
agtaagaatg atatttcccc ccagggatca ccaaatttt ataaaaattt gt 112

<210> 127
<211> 54
<212> DNA
<213> Homo sapien

<400> 127
accacgaaac cacaacaag atggaagcat caatccactt gccagcaca gcag 54

<210> 128
<211> 323
<212> DNA
<213> Homo sapien

<400> 128
acctcattag taattgtttt gttgtttcat ttttttctaa tgtctcccct ctaccagctc 60
acctgagata acagaatgaa aatggaagga cagccagatt tctcctttgc tctctgctca 120
ttctctctga agtctaggtt acccattttg gggaccatt ataggcaata aacacagttc 180

ccaaagcatt tggacagttt cttgtttgtg tttagaatgg ttttcctttt tcttagcctt 240
 ttcttgcaaa aggcctcactc agtcccttgc ttgctcagtg gactgggctc cccagggcct 300
 aggtgcctt cttttccatg tcc 323

<210> 129
 <211> 192
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(192)
 <223> n = A,T,C or G

<400> 129
 acatacatgt gtgtatatatt ttaaatatca cttttgtatc actctgactt tttagcatac 60
 tgaaaacaca ctaacataat ttntgtgaac catgatcaga tacaacccaa atcattcatc 120
 tagcacattc atctgtgata naaagatagg tgagtttcat ttccttcacg ttggccaatg 180
 gataaacaaa gt 192

<210> 130
 <211> 362
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(362)
 <223> n = A,T,C or G

<400> 130
 ccctttttta tggaatgagt agactgtatg tttgaanatt tanccacaac ctctttgaca 60
 tataatgacg caacaaaaag gtgctgttta gtcctatggg tcagtttatg cccctgacaa 120
 gtttccattg tgttttgccg atcttctggc taatcgtggg atcctccatg ttattagtaa 180
 ttctgtattc cattttgtta acgcctggta gatgtaacct gctangaggc taactttata 240
 cttattttaa agctcttatt ttgtgggtcat taaaatggca atttatgtgc agcactttat 300
 tgcagcagga agcacgtgtg gggttggttg aaagctcttt gctaattcta aaaagtaatg 360
 gg 362

<210> 131
 <211> 332
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(332)
 <223> n = A,T,C or G

<400> 131
 ctttttgaag gatcgtgtcc actcctgtgg acatcttgtt ttaatggagt ttcccatgca 60
 gtangactgg tatggttgca gctgtccaga taaaaacatt tgaagagctc caaaatgaga 120
 gttctcccag gttcgccctg ctgctccaag tctcagcagc agcctctttt aggaggcatc 180
 ttctgaacta gattaaggca gcttgtaaat ctgatgtgat ttgggtttatt atccaactaa 240

cttccatctg ttatcactgg agaaagccca gactcccan gacnggtacg gattgtgggc 300
atanaaggat tgggtgaagc tggcgttgtg gt 332

<210> 132
<211> 322
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(322)
<223> n = A,T,C or G

<400> 132
acttttgcca ttttgtatat ataaacaatc ttgggacatt ctctgaaaa ctagggtgcc 60
agtggctaag agaactcgat ttcaagcaat tctgaaagga aaaccagcat gacacagaat 120
ctcaaattcc caaacagggg ctctgtggga aaaatgaggg aggacctttg tatctcgggt 180
tttagcaagt taaaatgaan atgacaggaa aggcttattt atcaacaaag agaagagttg 240
ggatgcttct aaaaaaaact ttggtagaga aaataggaat gctnaatcct agggaagcct 300
gtaacaatct acaattgggc ca 322

<210> 133
<211> 278
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(278)
<223> n = A,T,C or G

<400> 133
acaagccttc acaagtttaa ctaaattggg attaatcttt ctgtanttat ctgcataatt 60
cttgtttttc tttccatctg gctcctgggt tgacaatttg tggaaacaac tctattgcta 120
ctatttaaaa aaaatcacaa atctttccct ttaagctatg ttnaattcaa actattcctg 180
ctattcctgt tttgtcaaag aaattatatt tttcaaaata tgtntatttg tttgatgggt 240
cccacgaaac actaataaaa accacagaga ccagcctg 278

<210> 134
<211> 121
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(121)
<223> n = A,T,C or G

<400> 134
gtttanaaaa cttgtttagc tccatagagg aaagaatggt aaactttgta ttttaaaaca 60
tgattctctg aggttaaact tgggtttcaa atgttatatt tacttgtatt ttgcttttgg 120
t 121

<210> 135

006230"006230"

<211> 350
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(350)
 <223> n = A,T,C or G

<400> 135
 acttanaacc atgcctagca catcagaatc cctcaaagaa catcagtata atcctataacc 60
 atancaagtg gtgactgggt aagcgtgcga caaaggtcag ctggcacatt acttgtgtgc 120
 aaacttgata cttttgttct aagtaggaac tagtatacag tncctaggan tggtagtcca 180
 ggggtccccc caactcctgc agccgctcct ctgtgccagn ccctgnaagg aactttcgct 240
 ccacctcaat caagccctgg gccatgctac ctgcaattgg ctgaacaaac gtttgctgag 300
 ttcccaagga tgcaagcct ggtgctcaac tcctggggcg tcaactcagt 350

<210> 136
 <211> 399
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(399)
 <223> n = A,T,C or G

<400> 136
 tgtaccgtga agacgacaga agttgcatgg caggggacagg gcaggggccga ggccaggggtt 60
 gctgtgattg tatccgaata ntccctgtga gaaaagataa tgagatgacg tgagcagcct 120
 gcagacttgt gtctgccttc aanaagccag acaggaaggc cctgcctgcc ttggctctga 180
 cctggcggcc agccagccag ccacaggtgg gcttcttctt tttgtggtga caacnccaag 240
 aaaactgcag aggccagggt tcaggtgtga gtgggtangt gaccataaaa caccaggtgc 300
 tcccaggaac ccgggcaaag gccatcccca cctacagcca gcatgcccac tggcgtgatg 360
 ggtgcagang gatgaagcag ccagntgttc tgctgtggt 399

<210> 137
 <211> 165
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(165)
 <223> n = A,T,C or G

<400> 137
 actggtgtgg tngggggtga tgctggtggt anaagttgan gtgacttcan gatggtgtgt 60
 ggaggaagtg tgtgaacgta gggatgtaga ngttttggcc gtgctaaatg agcttcggga 120
 ttggctggtc ccactggtgg tcaactgtcat tgggtggggt cctgt 165

<210> 138
 <211> 338
 <212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(338)

<223> n = A,T,C or G

<400> 138

actcactgga	atgccacatt	cacaacagaa	tcagaggtct	gtgaaaacat	taatggctcc	60
ttaacttctc	cagtaagaat	cagggacttg	aaatggaaac	gttaacagcc	acatgcccac	120
tgctggggcag	tctcccatgc	cttccacagt	gaaagggctt	gagaaaaatc	acatccaatg	180
tcattgtgttt	ccagccacac	caaaagggtgc	ttgggggtgga	gggctggggg	catananggt	240
cangcctcag	gaagcctcaa	gttccattca	gctttgccac	tgtacattcc	ccatntttta	300
aaaaactgat	gccttttttt	tttttttttg	taaaattc			338

<210> 139

<211> 382

<212> DNA

<213> Homo sapien

<400> 139

gggaatcttg	gtttttggca	tctggtttgc	ctatagccga	ggccactttg	acagaacaaa	60
gaaagggact	tcagtaaga	aggtgattta	cagccagcct	agtgcccgaa	gtgaaggaga	120
attcaaacag	acctcgtcat	tcttgggtgtg	agcctgggtcg	gtcaccgcc	tatcatctgc	180
atttgcttta	ctcaggtgct	accggactct	ggcccttgat	gtctgtagtt	tcacaggatg	240
ccttatttgt	cttctacacc	ccacagggcc	cctacttct	tcggatgtgt	ttttaataat	300
gtcagctatg	tgccccatcc	tccttcatgc	cctccctccc	tttccctacca	ctgctgagtg	360
gcctggaact	tgtttaaagt	gt				382

<210> 140

<211> 200

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(200)

<223> n = A,T,C or G

<400> 140

accaaancctt	ctttctgttg	tgttngattt	tactataggg	gtttngcttn	ttctaaanat	60
acttttcatt	taacancttt	tgtaagtgt	caggctgcac	tttgctccat	anaattattg	120
ttttcacatt	tcaacttgta	tgtgtttgtc	tcttanagca	ttgggtgaaat	cacatatttt	180
atattcagca	taaaggagaa					200

<210> 141

<211> 335

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(335)

<223> n = A,T,C or G

```

<400> 141
actttatttt caaaacactc atatgttgca aaaaacacat agaaaaataa agtttggtgg      60
gggtgctgac taaacttcaa gtcacagact tttatgtgac agattggagc agggtttggt      120
atgcatgtag agaaccctaa ctaatttatt aaacaggata gaaacaggct gtctgggtga      180
aatggttctg agaaccatcc aattcacctg tcagatgctg atanactagc tcttcagatg      240
tttttctacc agttcagaga tnggttaatg actantttcca atggggaaaa agcaagatgg      300
attcacaacac caagtaattt taaacaaaga cactt                                335

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<210> 142
<211> 459
<212> DNA
<213> Homo sapien

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<220>
<221> misc_feature
<222> (1)...(459)
<223> n = A,T,C or G

```

```

<400> 142
accagggttaa tattgccaca tatatccttt ccaattgcgg gctaaacaga cgtgtattta      60
gggttggttta aagacaaccc agcttaatat caagagaaat tgtgaccttt catggagtat      120
ctgatggaga aaacactgag ttttgacaaa tcttatttta ttcagatagc agtctgatca      180
cacatgggtcc aacaacactc aaataataaa tcaaataatna tcagatgtta aagattgggtc      240
ttcaaacatc atagccaatg atgccccgct tgcctataat ctctccgaca taaaaccaca      300
tcaacacctc agtggccacc aaaccattca gcacagcttc cttaactgtg agctgtttga      360
agctaccagt ctgagcacta ttgactatnt ttttcangct ctgaatagct ctagggatct      420
cagcanggggt gggaggaacc agctcaacct tggcgctant                                459

```

```

<210> 143
<211> 140
<212> DNA
<213> Homo sapien

```

```

<400> 143
acatttcctt ccaccaagtc aggactcctg gcttctgtgg gagttcttat cacctgaggg      60
aatccaaac agtctctcct agaaaggaat agtgtcacca accccaccca tctccctgag      120
accatccgac ttccctgtgt                                140

```

```

<210> 144
<211> 164
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(164)
<223> n = A,T,C or G

```

```

<400> 144
acttcagtaa caacatacaa taacaacatt aagtgtatat tgccatcttt gtcattttct      60
atctatacca ctctcccttc tgaaaacaan aatcactanc caatcactta tacaaatttg      120
aggcaattaa tccatatttg ttttcaataa ggaaaaaaag atgt                                164

```

<210> 145
 <211> 303
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(303)
 <223> n = A,T,C or G

<400> 145
 acgtagacca tccaactttg tatttgtaat ggcaaacatc cagnagcaat tcctaaacaa 60
 actggaggggt atttataccc aattatoccc ttcatthaaca tgccctcctc ctcaggctat 120
 gcaggacagc tatcataagt cggcccaggc atccagatac taccatttgt ataaacttca 180
 gtaggggagt ccatccaagt gacagggtcta atcaaaggag gaaatggaac ataagcccag 240
 tagtaaaatn ttgcttagct gaaacagcca caaaagactt accgccgtgg tgattaccat 300
 caa 303

<210> 146
 <211> 327
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(327)
 <223> n = A,T,C or G

<400> 146
 actgcagctc aattagaagt ggtctctgac ttatcatcanc ttctccctgg gctccatgac 60
 actggcctgg agtgactcat tgctctgggt gggttgagaga gctcctttgc caacaggcct 120
 ccaagtcagg gctgggattt gtttcctttc cacattctag caacaatatg ctggccactt 180
 cctgaacagg gaggggtggga ggagccagca tgggaacaagc tgccactttc taaagtagcc 240
 agacttgccc ctgggcctgt cacacctact gatgaccttc tgtgcctgca ggatggaatg 300
 taggggtgag ctgtgtgact ctatgggt 327

<210> 147
 <211> 173
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(173)
 <223> n = A,T,C or G

<400> 147
 acattgtttt ttgagataa agcattgana gagctctcct taacgtgaca caatggaagg 60
 actggaacac ataccacat ctttgttctg agggataatt ttctgataaa gtcttgctgt 120
 atattcaagc acatatgtta tatattattc agttccatgt ttatagccta gtt 173

<210> 148
 <211> 477
 <212> DNA

006230 362550

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(477)

<223> n = A,T,C or G

<400> 148

acaaccactt	tatctcatcg	aattttttaac	ccaaactcac	tcactgtgcc	tttctatcct	60
atgggatata	ttatttgatg	ctccatttca	tcacacatat	atgaataata	cactcatact	120
gccctactac	ctgctgcaat	aatcacattc	ccttcctgtc	ctgaccctga	agccattggg	180
gtgggtcctag	tggccatcag	tccangcctg	caccttgagc	ccttgagctc	cattgctcac	240
nccancccac	ctcaccgacc	ccatcctctt	acacagctac	ctccttgctc	tctaacccca	300
tagattatnt	ccaaattcag	tcaattaagt	tactattaac	actctacccg	acatgtccag	360
caccactggg	aagccttctc	cagccaacac	acacacacac	acacncacac	acacacatat	420
ccaggcacag	gctacctcat	cttcacaatc	acccctttaa	ttaccatgct	atggtgg	477

<210> 149

<211> 207

<212> DNA

<213> Homo sapien

<400> 149

acagttgtat	tataatatca	agaaataaac	ttgcaatgag	agcattttaag	agggaagaac	60
taacgtattt	tagagagcca	aggaagggtt	ctgtggggag	tgggatgtaa	ggtggggcct	120
gatgataaat	aagagtcagc	caggtaagt	ggtggtgtgg	tatgggcaca	gtgaagaaca	180
tttcaggcag	agggaacacg	agtgaaa				207

<210> 150

<211> 111

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(111)

<223> n = A,T,C or G

<400> 150

accttgattt	cattgctgct	ctgatggaaa	cccaactatc	taatttagct	aaaacatggg	60
cacttaaattg	tggtcagtgt	ttggacttgt	taactantgg	catctttggg	t	111

<210> 151

<211> 196

<212> DNA

<213> Homo sapien

<400> 151

agcgcggcag	gtcatattga	acattccaga	tacctatcat	tactcgatgc	tgttgataac	60
agcaagatgg	ctttgaactc	agggtcacca	ccagctattg	gaccttacta	tgaaaaccat	120
ggataccaac	cggaaaaccc	ctatcccgc	cagcccactg	tgggtccccc	tgtctacgag	180
gtgcatccgg	ctcagt					196

<210> 152

<400> 155						
actggaaata	ataaaaccca	catcacagtg	ttgtgtcaaa	gatcatcagg	gcatggatgg	60
gaaagtgctt	tgggaactgt	aaagtgccta	acacatgata	gatgattttt	gttataatat	120
ttgaatcacg	gtgcatacaa	actctctctg	ctgctctctc	tgggccccc	ccccagcccc	180
atcacagctc	actgctctgt	tcatccaggc	ccagcatgta	gtggctgatt	cttcttggct	240

gcttttagcc tccanaagtt tctctgaagc caaccaaacc tctangtgta aggcatgctg 300
gccctggg 308

<210> 156
<211> 295
<212> DNA
<213> Homo sapien

<400> 156
accttgctcg gtgcttggaa catattagga actcaaaata tgagatgata acagtgccta 60
ttattgatta ctgagagaac tgttagacat ttagttgaag attttctaca caggaaactga 120
gaataggaga ttatgttttg ccctcatatt ctctcctatc ctcttgcct cattctatgt 180
ctaatatatt ctcaatcaaa taaggtttagc ataatcagga aatcgaccaa ataccaatat 240
aaaaccagat gtctatcctt aagattttca aatagaaaac aaattaacag actat 295

<210> 157
<211> 126
<212> DNA
<213> Homo sapien

<400> 157
acaagtttaa atagtgtgt cactgtgcat gtgctgaaat gtgaaatcca ccacatttct 60
gaagagcaaa acaaattctg tcatgtaatc tctatcttgg gtcgtgggta tatctgtccc 120
cttagt 126

<210> 158
<211> 442
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(442)
<223> n = A,T,C or G

<400> 158
accactgggt cttggaaca cccatcctta atacgatgat ttttctgtcg tgtgaaaatg 60
aanccagcag gctgccccta gtcagtcctt ccttccagag aaaaagagat ttgagaaagt 120
gcctgggtaa ttcaccatta atttcctccc ccaaactctc tgagtcttcc cttaatat 180
ctggtggttc tgaccaaagc aggtcatggg ttgttgagca tttgggatcc cagtgaagta 240
natgtttgta gccttgcata cttagccctt cccacgcaca aacggagtgg cagagtggg 300
ccaacctgt tttccagtc cacgtagaca gattcacagt gcggaattct ggaagctgga 360
nacagacggg ctctttgcag agccgggact ctgagangga catgagggcc tctgcctctg 420
tgttcattct ctgatgtcct gt 442

<210> 159
<211> 498
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(498)
<223> n = A,T,C or G

```

<400> 159
acttccaggt aacgttggtg tttccgttga gcctgaactg atgggtgacg ttgtaggttc      60
tccaacaaga actgagggtg cagagcgggt agggaagagt gctgttccag ttgcacctgg      120
gctgctgtgg actgttggtg attcctcact acggcccaag gttgtggaac tggcanaaaag      180
gtgtgttggt gganttgagc tcgggcgggt gtggtagggt gtgggctctt caacaggggc      240
tgctgtggtg ccgggangtg aangtggtgt gtcacttgag cttggccagc tctggaaagt      300
antanattct tectgaaggc cagcgcctgt ggagctggca ngggtcantg ttgtgtgtaa      360
cgaaccagtg ctgctgtggg tgggtgtana tcctccacaa agcctgaagt tatggtgtcn      420
tcaggtaana atgtggtttc agtgtccctg ggcngctgtg gaaggttgta nattgtcacc      480
aagggaataa gctgtggt

```

```

<210> 160
<211> 380
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(380)
<223> n = A,T,C or G

```

```

<400> 160
acctgcatcc agcttccctg ccaaactcac aaggagacat caacctctag acagggaaac      60
agcttcagga tacttccagg agacagagcc accagcagca aaacaaatat tcccatgcct      120
ggagcatggc atagaggaag ctganaaatg tggggtctga ggaagccatt tgagtctggc      180
cactagacat ctcatcagcc acttgtgtga agagatgcc catgaccca gatgcctctc      240
ccacccttac ctccatctca cacacttgag ctttccactc tgtataattc taacatcctg      300
gagaaaaatg gcagtttgac cgaacctgtt cacaacggta gaggttgatt tctaacgaaa      360
cttgtagaat gaagcctgga

```

```

<210> 161
<211> 114
<212> DNA
<213> Homo sapien

```

```

<400> 161
actccacatc ccctctgagc aggcggttgt cgttcaaggt gtatttggcc ttgcctgtca      60
cactgtccac tggccctta tccacttggt gcttaatccc tcgaaagagc atgt      114

```

```

<210> 162
<211> 177
<212> DNA
<213> Homo sapien

```

```

<400> 162
actttctgaa tcgaatcaaa tgatacttag tgtagtttta atatcctcat atatatcaaa      60
gttttactac tctgataatt ttgtaaacca ggtaaccaga acatccagtc atacagcttt      120
tgggtgatata taacttggca ataaccagc ctggtgatac ataaaactac tcactgt      177

```

```

<210> 163
<211> 137
<212> DNA
<213> Homo sapien

```

<220>
 <221> misc_feature
 <222> (1)...(137)
 <223> n = A,T,C or G

<400> 163
 catttatata gacaggcgtg aagacattca cgacaaaaac gcgaaattct atccccgtgac 60
 canagaaggc agctacggct actcctacat cctggcgtgg gtggccttcg cctgcacctt 120
 catcagcggc atgatgt 137

<210> 164
 <211> 469
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(469)
 <223> n = A,T,C or G

<400> 164
 cttatcacaa tgaatgttct cctgggcagc gttgtgatct ttgccacctt cgtgacttta 60
 tgcaatgcat catgctatct catacctaata gagggagttc caggagattc aaccaggaaa 120
 tgcattggatc tcaaaggaaa caaacaccca ataaactcgg agtggcagac tgacaactgt 180
 gagacatgca cttgctacga aacagaaatt tcatgttgca cccttgtttc tacacctgtg 240
 gggttatgaca aagacaactg ccaaagaatc ttcaagaagg aggactgcaa gtatatcgtg 300
 gtggagaaga aggacccaaa aaagacctgt tctgtcagtg aatggataat ctaatgtgct 360
 tctagttagc acaggggctcc caggccaggc ctcattctcc tctggcctct aatagtcaat 420
 gattgtgtag ccatgcctat cagtaaaaag atntttgagc aaacacttt 469

<210> 165
 <211> 195
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(195)
 <223> n = A,T,C or G

<400> 165
 acagtttttt atanatatcg acattgccgg cacttgtggt cagtttcata aagctgggtg 60
 atccgctgtc atccactatt ccttggctag agtaaaaatt attcttatag cccatgtccc 120
 tgcaggcgc cgcgccgtag ttctcggtcc agtcgtcttg gcacacaggg tgccaggact 180
 tcctctgaga tgagt 195

<210> 166
 <211> 383
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature

<222> (1)...(383)

<223> n = A,T,C or G

<400> 166

```
acatcttagt agtgtggcac atcagggggc catcagggtc acagtcactc atagcctcgc      60
cgaggtcgga gtccacacca ccggtgtagg tgtgtctcaat cttgggcttg gcgcccacct      120
ttggagaagg gatatgctgc acacacatgt ccacaaagcc tgtgaactcg ccaaagaatt      180
tttgacagacc agcctgagca aggggcggat gttcagcttc agtcctcct tgcgcaggtg      240
gatgccaacc tcgtctangg tccgtgggaa gctgggtgtcc acntcaccta caacctgggc      300
gangatctta taaagaggct ccnagataaa ctccacgaaa cttctctggg agctgctagt      360
nggggccttt ttggtgaact ttc                                     383
```

<210> 167

<211> 247

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(247)

<223> n = A,T,C or G

<400> 167

```
acagagccag accttggcca taaatgaanc agagattaag actaaacccc aagtcganat      60
tgagagcagaa actggagcaa gaagtgggcc tggggctgaa gtagagacca aggccactgc      120
tatanccata cacagagcca actctcaggc caaggcnatg gttggggcag anccagagac      180
tcaatctgan tccaaagtgg tggctggaac actggtcatg acanaggcag tgactctgac      240
tganctc                                     247
```

<210> 168

<211> 273

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(273)

<223> n = A,T,C or G

<400> 168

```
acttctaagt tttctagaag tggaaggatt gtantcatcc tgaaaatggg tttacttcaa      60
aatccctcan ccttgttctt cacnactgtc tatactgana gtgtcatgtt tccacaaagg      120
gctgacacct gagcctgnat tttcactcat ccctgagaag ccctttccag taggggtggc      180
aattcccaac ttccttgcca caagcttccc aggcctttctc ccctggaaaa ctccagcttg      240
agtccagat acactcatgg gctgccctgg gca                                     273
```

<210> 169

<211> 431

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(431)

<223> n = A,T,C or G

<400> 169

acagccttgg	cttccccaaa	ctccacagtc	tcagtgcaga	aagatcatct	tccagcagtc	60
agctcagacc	aggggtcaaag	gatgtgacat	caacagtttc	tggtttcaga	acaggttcta	120
ctactgtcaa	atgaccccc	atacttcctc	aaaggctgtg	gtaagttttg	cacagggtgag	180
ggcagcagaa	aggggggtant	tactgatgga	caccatcttc	tctgtatact	ccacactgac	240
cttgccatgg	gcaaaggccc	ctaccacaaa	aacaatagga	tcactgctgg	gcaccagctc	300
acgcacatca	ctgacaaccg	ggatggaaaa	agaantgcca	actttcatac	atccaactgg	360
aaagtgatct	gatactggat	tcttaattac	cttcaaaagc	ttctgggggc	catcagctgc	420
tcgaacactg	a					431

<210> 170

<211> 266

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(266)

<223> n = A,T,C or G

<400> 170

acctgtgggc	tgggctgtta	tgccctgtgc	ggctgctgaa	agggagttca	gaggtggagc	60
tcaaggagct	ctgcaggcat	tttgccaanc	ctctccanag	canagggagc	aacctacact	120
ccccgctaga	aagacaccag	attggagctc	tgggaggggg	agttgggggtg	ggcatttgat	180
gtatacttgt	cacctgaatg	aangagccag	agaggaanga	gacgaanatg	anattggcct	240
tcaaagctag	gggtctggca	ggtgga				266

<210> 171

<211> 1248

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(1248)

<223> n = A,T,C or G

<400> 171

ggcagccaaa	tcataaacgg	cgaggactgc	agcccgcact	cgcagccctg	gcaggcggca	60
ctggtcatgg	aaaacgaatt	gttctgctcg	ggcgtcctgg	tgcattccgca	gtgggtgctg	120
tcagccgcac	actgtttcca	gaagtgagtg	cagagctcct	acaccatcgg	gctgggcctg	180
cacagtcttg	aggccgacca	agagccaggg	agccagatgg	tggaggccag	cctctccgta	240
cggcacccag	agtacaacag	acccttgctc	gctaacgacc	tcatgctcat	caagttggac	300
gaatccgtgt	ccgagtctga	caccatccgg	agcatcagca	ttgcttcgca	gtgccctacc	360
gcggggaaact	cttgccctcg	ttctggctgg	ggtctgctgg	cgaacggcag	aatgcctacc	420
gtgctgcagt	gcgtgaacgt	gtcggtggtg	tctgaggagg	tctgcagtaa	gctctatgac	480
ccgctgtacc	accccagcat	gttctgcgcc	ggcggagggg	aagaccagaa	ggactcctgc	540
aacggtgact	ctggggggcc	cctgatctgc	aacgggtact	tgcagggcct	tgtgtctttc	600
ggaaaagccc	cgtgtggcca	agttggcgtg	ccagggtgtc	acaccaacct	ctgcaaattc	660
actgagtggg	tagagaaaac	cgtccaggcc	agttaactct	ggggactggg	aacccatgaa	720
attgaccccc	aaatacatcc	tgcggaagga	attcaggaat	atctgttccc	agccccctct	780
ccctcaggcc	caggagtcca	ggcccccagc	ccctcctccc	tcaaaccaag	ggtacagatc	840

```

cccagccctt cctccctcag acccaggagt ccagaccccc cagccctcc tccctcagac 900
ccaggagtcc agcccctcct ccctcagacc caggagtcca gacccccag cccctcctcc 960
ctcagaccca ggggtccagg cccccaaccc ctcctccctc agactcagag gtccaagccc 1020
ccaaccntc attccccaga cccagaggtc cagggtcccag cccctcntcc ctcagaccca 1080
gcggtccaat gccacctaga ctntccctgt acacagtgcc cccttggtgc acgttgaccc 1140
aaccttacca gttggttttt catttttngt ccctttcccc tagatccaga aataaagttt 1200
aagagaagng caaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaa 1248

```

```

<210> 172
<211> 159
<212> PRT
<213> Homo sapien

```

```

<220>
<221> VARIANT
<222> (1)...(159)
<223> Xaa = Any Amino Acid

```

```

<400> 172
Met Val Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro
1          5          10          15
Leu Leu Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser
20          25          30
Glu Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr
35          40          45
Ala Gly Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly
50          55          60
Arg Met Pro Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu
65          70          75          80
Glu Val Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe
85          90          95
Cys Ala Gly Gly Gly Gln Xaa Gln Xaa Asp Ser Cys Asn Gly Asp Ser
100         105         110
Gly Gly Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe
115         120         125
Gly Lys Ala Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn
130         135         140
Leu Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser
145         150         155

```

```

<210> 173
<211> 1265
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(1265)
<223> n = A,T,C or G

```

```

<400> 173
ggcagcccg actgcagcc ctggcaggcg gcaactgggtca tggaaaacga attgttctgc 60
tcgggcgtcc tgggtcatcc gcagtgggtg ctgtcagccg cacactgttt ccagaactcc 120
tacaccatcg ggctgggcct gcacagtctt gagggccgacc aagagccagg gagccagatg 180

```

```

gtggaggcca gcctctccgt acggcaccca gagtacaaca gacccttgct cgctaacgac 240
ctcatgctca tcaagttgga cgaatccgtg tccgagtctg acaccatccg gagcatcagc 300
attgcttcgc agtgccttac cgcggggaac tcttgccctg tttctggctg gggctctgctg 360
gcgaacgggtg agctcacggg tgtgtgtctg ccctcttcaa ggaggtcctc tgcccagtcg 420
cgggggctga cccagagctc tgcgtcccag gcagaatgcc taccgtgctg cagtgcgtga 480
acgtgtcggg ggtgtctgag gaggtctgca gtaagctcta tgaccgctg taccaccca 540
gcatgttctg cgcggcgga gggcaagacc agaaggactc ctgcaacggg gactctgggg 600
ggcccctgat ctgcaacggg tacttgacgg gccttgctgc tttcgaaaa gcccgtgtg 660
gccaagttgg cgtgccagg gtctacacca acctctgcaa attcactgag tggatagaga 720
aaaccgtcca ggccagttaa ctctggggac tgggaaccca tgaaattgac ccccaaatac 780
atcctgcgga aggaattcag gaatatctgt tcccagcccc tcctccctca ggcccaggag 840
tccaggcccc cagccccctc tcctcaaac caagggtaca gatccccagc ccctcctccc 900
tcagaccagc gagtcacagc cccccagccc ctctccctc agaccagga gtccagcccc 960
tcctccntca gaccaggag tcacagcccc ccagccctc ctccctcaga cccaggggtt 1020
gaggccccca acccctctc ctccagagtc agagggtcaa gcccacaacc cctcgttccc 1080
cagaccagga ggtnnaggtc ccagccctc ttcctcaga cccagnggtc caatgccacc 1140
tagattttcc ctgnacacag tgcccccttg tggngangttg acccaacctt accagttggg 1200
ttttcatttt tngtcccttt cccctagatc cagaaataaa gtttaagaga nngcaaaaa 1260
aaaaa 1265

```

```

<210> 174
<211> 1459
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(1459)
<223> n = A,T,C or G

```

```

<400> 174
ggtcagccgc acactgtttc cagaagtggg tgcagagctc ctacaccatc gggctggggc 60
tgcacagtct tgaggccgac caagagccag ggagccagat ggtggaggcc agcctctccg 120
tacggcacc agagtacaac agacccttg tgcgtaacga cctcatgctc atcaagttgg 180
acgaatccgt gtccgagtct gacaccatcc ggagcatcag cattgcttcg cagtgcctta 240
ccgcggggaa ctcttgctc gtttctggct ggggtctgct ggcgaacggg gagctcacgg 300
gtgtgtgtct gccctcttca aggaggtcct ctgcccagtc gcgggggctg acccagagct 360
ctgctgctcca ggcagaatgc ctaccgtgct gcagtgcgtg aacgtgtcgg tgggtgtctga 420
ngagggtctg antaagctct atgaccgct gtaccacccc ancatgttct gcgccggcgg 480
agggcaagac cagaaggact cctgcaacgt gagagagggg aaaggggagg gcaggcgact 540
caggggaagg tggagaagg ggagacagag acacacaggg ccgcatggcg agatgcagag 600
atggagagac acacaggag acagtgacaa ctagagagag aaactgagag aaacagagaa 660
ataaacacag gaataaagag aagcaaagga agagagaaac agaaacagac atggggaggc 720
agaaacacac acacatagaa atgcagttga ccttccaaca gcatggggcc tgagggcggg 780
gacctccacc caatagaaaa tcctcttata acttttgact ccccaaaaac ctgactagaa 840
atagcctact gttgacggg agccttacca ataacataaa tagtcgattt atgcatacgt 900
tttatgcatt catgatatac ctttgttgga attttttgat atttctaagc tacacagttc 960
gtctgtgaat ttttttaaat tgttgcaact ctctaaaaat ttttctgatg tgtttattga 1020
aaaaatccaa gtataagtgg acttgtgcat tcaaaccagg gttgttcaag ggtcaactgt 1080
gtaccagag ggaaacagtg acacagattc atagaggtga aacacgaaga gaaacaggaa 1140
aatcaagac tctacaaaga ggctgggcag ggtggctcat gcctgtaatc ccagcacttt 1200
gggaggcgag gcaggcagat cacttgaggt aaggagttca agaccagcct ggccaaaatg 1260
gtgaaatcct gtctgtacta aaaatacaaa agttagctgg atatggtggc aggcgcctgt 1320
aatcccagct acttgggagg ctgaggcagg agaattgctt gaatatggga ggcagaggtt 1380

```



```
gaagtgagtt gagatcacac cactatactc cagctggggc aacagagtaa gactctgtct 1440
caaaaaaaaa aaaaaaaaaa 1459
```

```
<210> 175
<211> 1167
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(1167)
<223> n = A,T,C or G
```

```
<400> 175
gcgcagccct ggcaggcggc actggtcatg gaaaacgaat tgttctgctc gggcgtcctg 60
gtgcatccgc agtgggtgct gtcagccgca cactgtttcc agaactccta caccatcggg 120
ctgggcctgc acagtcttga ggccgaccaa gagccaggga gccagatggg ggaggccagc 180
ctctccgtac ggcacccaga gtacaacaga ctcttgctcg ctaacgacct catgctcatc 240
aagttggacg aatccgtgtc cgagtctgac accatccgga gcatcagcat tgcttcgcag 300
tgccctaccg cggggaactc ttgcctcgtn tctggctggg gtctgctggc gaacggcaga 360
atgcctaccg tgctgcactg cgtgaacgtg tcggtgggtg ctgaggangt ctgcagtaag 420
ctctatgacc cgctgtacca ccccagcatg ttctgcgccg gcggagggca agaccagaag 480
gactcctgca acggtgactc tggggggccc ctgatctgca acgggtactt gcagggcctt 540
gtgtctttcg gaaaagcccc gtgtggccaa cttggcgtgc cagggtgtcta caccaacctc 600
tgcaaattca ctgagtggat agagaaaacc gtccagncca gttaactctg gggactggga 660
acccatgaaa ttgaccccca aatacatcct gcggaangaa ttcaggaata tctgttccca 720
gcccctcctc cctcaggccc aggagtccag gccccagcc cctcctccct caaaccaagg 780
gtacagatcc ccagcccctc ctccctcaga cccaggagtc cagacccccc agcccctcnt 840
ccntcagacc caggagtcca gcccctcctc cntcagacgc aggagtccag accccccagc 900
ccntcntccg tcagacccag ggggtgcaggc ccccaacccc tcntccntca gagtcagagg 960
tccaagcccc caaccctctg ttccccagac ccagaggtnc aggtcccagc cctcctccc 1020
tcagaccag cggtccaatg ccacctagan tntccctgta cacagtgcc ccttggtggca 1080
ngttgacca accttaccag ttggtttttc attttttgtc cttttccctc agatccagaa 1140
ataaagtnta agagaagcgc aaaaaaa 1167
```

```
<210> 176
<211> 205
<212> PRT
<213> Homo sapien

<220>
<221> VARIANT
<222> (1)...(205)
<223> Xaa = Any Amino Acid
```

```
<400> 176
Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln Trp
 1             5             10             15
Val Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu
                20             25             30
Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val
                35             40             45
Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Leu Leu Leu
 50             55             60
```

Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser
 65 70 75 80
 Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly
 85 90 95
 Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg Met
 100 105 110
 Pro Thr Val Leu His Cys Val Asn Val Ser Val Val Ser Glu Xaa Val
 115 120 125
 Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys Ala
 130 135 140
 Gly Gly Gly Gln Asp Gln Lys Asp Ser Cys Asn Gly Asp Ser Gly Gly
 145 150 155 160
 Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly Lys
 165 170 175
 Ala Pro Cys Gly Gln Leu Gly Val Pro Gly Val Tyr Thr Asn Leu Cys
 180 185 190
 Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Xaa Ser
 195 200 205

<210> 177
 <211> 1119
 <212> DNA
 <213> Homo sapien

<400> 177
 gcgcactcgc agccctggca ggcggcactg gtcattggaaa acgaattggt ctgctcgggc 60
 gtccctggtgc atccgcagtg ggtgctgtca gccgcacact gtttccagaa ctccctacacc 120
 atcgggctgg gctgcacag tcttgaggcc gaccaagagc caggagacca gatggtggag 180
 gccagcctct ccgtacggca cccagagtac aacagaccct tgctcgctaa cgacctcatg 240
 ctcactcaagt tggacgaatc cgtgtccgag tctgacacca tccggagcat cagcattgct 300
 tcgcagtgcc ctaccgcggg gaactcttgc ctggtttctg gctggggtct gctggcgaac 360
 gatgctgtga ttgccatcca gtcccagact gtgggaggct gggagtgtga gaagctttcc 420
 caaccctggc agggttgtac catttcggca acttccagtg caaggacgtc ctgctgcac 480
 ctactgggt gctcactact gctcactgca tcaccggaa cactgtgatc aactagccag 540
 caccatagtt ctccgaagtc agactatcat gattactgtg ttgactgtgc tgtctattgt 600
 actaaccatg ccgatgttta ggtgaaatta gogtcaattg gcctcaacca tcttggtatc 660
 cagttatcct cactgaattg agatttcctg cttcagtgtc agccattccc acataatttc 720
 tgacctacag aggtgaggga tcatatagct ctccaaggat gctggtactc ccctcacaaa 780
 ttcattttctc ctgttgtagt gaaagggtgc ccctctggag cctcccaggg tgggtgtgca 840
 ggtcacaatg atgaatgtat gatcgtgttc ccattaccca aagccttta atccctcatg 900
 ctcatgtacac cagggcaggt ctagcatttc ttcatttagt gtatgctgtc cattcatgca 960
 accacctcag gactcctgga ttctctgcct agttgagctc ctgcatgctg cctccttggg 1020
 gaggtgaggg agagggccca tggttcaatg ggatctgtgc agttgtaaca cattaggtgc 1080
 ttaataaaca gaagctgtga tgtaaaaaa aaaaaaaaa 1119

<210> 178
 <211> 164
 <212> PRT
 <213> Homo sapien

<220>
 <221> VARIANT
 <222> (1)...(164)
 <223> Xaa = Any Amino Acid

006280" 006280" 006280"

<400> 178
 Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln Trp
 1 5 10 15
 Val Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu
 20 25 30
 Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val
 35 40 45
 Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu Leu
 50 55 60
 Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser
 65 70 75 80
 Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly
 85 90 95
 Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Asp Ala Val
 100 105 110
 Ile Ala Ile Gln Ser Xaa Thr Val Gly Gly Trp Glu Cys Glu Lys Leu
 115 120 125
 Ser Gln Pro Trp Gln Gly Cys Thr Ile Ser Ala Thr Ser Ser Ala Arg
 130 135 140
 Thr Ser Cys Cys Ile Leu Thr Gly Cys Ser Leu Leu Leu Thr Ala Ser
 145 150 155 160
 Pro Gly Thr Leu

<210> 179

<211> 250

<212> DNA

<213> Homo sapien

<400> 179

ctggagtgcc	ttggtgtttc	aagccctgc	aggaagcaga	atgcaccttc	tgaggcacct	60
ccagctgccc	ccggccggg	gatgcagggc	tggagcacc	cttgcccggc	tgtgattgct	120
gccaggcact	gttcatctca	gcttttctgt	ccctttgctc	ccggcaagcg	cttctgctga	180
aagttcatat	ctggagcctg	atgtcttaac	gaataaaggt	cccatgctcc	acccgaaaaa	240
aaaaaaaaaa						250

<210> 180

<211> 202

<212> DNA

<213> Homo sapien

<400> 180

actagtccag	tgtggtggaa	ttccattgtg	ttgggcccac	cacaatggct	acctttaaca	60
tcaccagac	cccggccctg	cccgctcccc	acgctgctgc	taacgacagt	atgatgctta	120
ctctgctact	cggaaactat	ttttatgtaa	ttaatgtatg	ctttcttggt	tataaatgcc	180
tgatttaaaa	aaaaaaaaaa	aa				202

<210> 181

<211> 558

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature
 <222> (1)...(558)
 <223> n = A,T,C or G

<400> 181
 tccytttgtk naggtttkkk agacamccck agacctwaan ctgtgtcaca gacttcyngg 60
 aatgttttagg cagtgtctagt aatttcytcg taatgattct gttattactt tcctnattct 120
 ttattcctct ttcttctgaa gattaatgaa gttgaaaatt gaggtggata aatacaaaaa 180
 ggtagtgtga tagtataagt atctaagtgc agatgaaagt gtgttatata tatccattca 240
 aaattatgca agtttagtaat tactcagggg taactaaatt actttaatat gctgttgaac 300
 ctactctgtt ccttggctag aaaaaattat aaacaggact ttgttagttt gggaagccaa 360
 attgataata ttctatgttc taaaagttgg gctatacata aattattaag aaatatggaw 420
 ttttattccc aggaatatgg kgttcatttt atgaatatta cscrggatag awgtwtgagt 480
 aaaaycagtt ttggtwaata ygtwaatatg tcmtaaataa acaakgcttt gacttatttc 540
 caaaaaaaaa aaaaaaaaa 558

<210> 182
 <211> 479
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(479)
 <223> n = A,T,C or G

<400> 182
 acagggwttk grggatgcta agsccccrga rwtggtttga tccaaccctg gcttwttttc 60
 agaggggaaa atggggccta gaagttacag mscatytagy tgggtgcgmg gcacccctgg 120
 cstcacacag astcccgagt agctgggact acaggcacac agtcaactgaa gcaggccctg 180
 ttwgcaattc acgttgccac ctccaactta aacattcttc atatgtgatg tccttagtca 240
 ctaagggttaa actttcccac ccagaaaagg caacttagat aaaatcttag agtactttca 300
 tactmttcta agtcctcttc cagcctcact kkgagtcctm cytggggggt gataggaant 360
 ntctcttggc tttctcaata aartctctat ycatctcatg tttaatttgg tacgcatara 420
 awtgstgara aaattaaaat gttctggtty mactttaaaa aaaaaaaaaa aaaaaaaaaa 479

<210> 183
 <211> 384
 <212> DNA
 <213> Homo sapien

<400> 183
 aggcgggagc agaagctaaa gccaaagccc aagaagagtg gcagtgccag cactggtgcc 60
 agtaccagta ccaataacag tgccagtgcc agtgccagca ccagtgggtg cttcagtgc 120
 ggtgccagcc tgaccgccac tctcacattt gggctcttcg ctggccttgg tggagctgg 180
 gccagcacca gtggcagctc tgggtgcctgt ggtttctcct acaagtgaga ttttagatat 240
 tgtaaatcct gccagtcttt ctcttcaagc cagggtgcat cctcagaaac ctactcaaca 300
 cagcactcta ggcagccact atcaatcaat tgaagttgac actctgcatt aratctattt 360
 gccatttcaa aaaaaaaaaa aaaa 384

<210> 184
 <211> 496
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(496)
 <223> n = A,T,C or G

<400> 184
 accgaattgg gaccgctggc ttataagcga tcatgtyynt ccrgtatcac ctcaacgagc 60
 agggagatcg agtctatacg ctgaagaaat ttgacccgat gggacaacag acctgctcag 120
 cccatcctgc tcggttctcc ccagatgaca aatactctsg acaccgaatc accatcaaga 180
 aacgcttcaa ggtgctcatg acccagcaac cgcgccctgt cctctgaggg tcccttaaag 240
 tgatgtcttt tctgccacct gttacccctc ggagactccg taaccaaaact cttcggactg 300
 tgagccctga tgcctttttg ccagccatac tctttggcat ccagtctctc gtggcgattg 360
 attatgcttg tgtgaggcaa tcatgggtggc atcacccata aagggaacac atttgacttt 420
 tttttctcat attttaaatt actacmagaw tattwmagaw waaatgawtt gaaaaactst 480
 taaaaaaaaa aaaaaa 496

<210> 185
 <211> 384
 <212> DNA
 <213> Homo sapien

<400> 185
 gctggtagcc tatggcgkgg cccacggagg ggctcctgag gccacggrac agtgacttcc 60
 caagtatcyt ggcsgcgtc ttctaccgtc cctacctgca gatcttcggg cagattcccc 120
 aggaggacat ggacgtggcc ctcatggagc acagcaactg ytcgtcggag cccggcttct 180
 gggcacaccc tcctggggcc caggcgggca cctgcgtctc ccagtatgcc aactggctgg 240
 tgggtgctgt cctcgtcatc ttctgctcgt tggccaacat cctgctggtc aacttgctca 300
 ttgccatgtt cagttacaca ttcggtcaaag tacagggcaa cagcgtatctc tactgggaag 360
 gcgcagcgtt accgcctcat ccgg 384

<210> 186
 <211> 577
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(577)
 <223> n = A,T,C or G

<400> 186
 gagttagctc ctccacaacc ttgatgaggt cgtctgcagt ggcctctcgc ttcataccgc 60
 tnccatcgtc atactgtagg tttgccacca cytcctggca tcttggggcg gcntaatatt 120
 ccaggaaact ctcaatcaag tcaccgtoga tgaaacctgt gggctgggtc tgtcttcgcg 180
 tcgggtgtgaa aggatctccc agaaggagtg ctogatcttc cccacacttt tgatgacttt 240
 attgagtcga ttctgcatgt ccagcaggag gttgtaccag ctctctgaca gtgaggtcac 300
 cagccctatc atgcggttga mcgtgccgaa garcaccgag ccttggtgtg gggkkgag 360
 ctcaccaga ttctgcatta ccagagagcc gtggcaaaaag acattgacaa actcgcaccag 420
 gtggaaaaag amcamctcct ggargtgctn gccgctcctc gtcmgttggt ggcagcgtw 480
 tccttttgac acacaaacaa gttaaaggca ttttcagccc ccagaaantt gtcatcatcc 540
 aagatntcgc acagcactna tccagttggg attaaat 577

<210> 187

<211> 534
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(534)
 <223> n = A,T,C or G

<400> 187
 aacatcttcc tgtataatgc tgtgtaatat cgatccgatn ttgtctgstg agaatycatw 60
 actkggaaaa gmaacattaa agcctggaca ctggtattaa aattcacaat atgcaacact 120
 ttaaacagtg tgtcaatctg ctcccyynac tttgtcatca ccagtctggg aakaagggta 180
 tgccctattc acacctgtta aaagggcgct aagcattttt gattcaacat cttttttttt 240
 gacacaagtc cgaaaaaagc aaaagtaaac agttatyaat ttgttagcca attcactttc 300
 ttcattgggac agagccatyt gatttaaaaa gcaaattgca taatattgag ctttygggagc 360
 tgatatattga gcggaagagt agcctttcta cttcaccaga cacaactccc tttcatattg 420
 ggatgttnac naaagtwatg tctctwacag atgggatgct tttgtggcaa ttctgttctg 480
 aggatctccc agtttattta ccacttgcac aagaaggcgt tttcttcctc aggc 534

<210> 188
 <211> 761
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(761)
 <223> n = A,T,C or G

<400> 188
 agaaaccagt atctctnaaa acaacctctc ataccttgtg gacctaatth ttgtgtgcgtg 60
 ttgtgtgtgcg cgcataattat atagacaggc acatcttttt tactttttgta aaagcttatg 120
 cctcttttgt atctatatct gtgaaagttt taatgatctg ccataatgtc ttggggacct 180
 ttgtcttctg tgtaaatggg actagagaaa acacctatnt tatgagtcaa tctagttngt 240
 tttattcgac atgaaggaaa tttccagatn acaacactna caaactctcc ctkgackarg 300
 ggggacaaaag aaaagcaaaa ctgamcataa raaacaatwa cctgggtgaga arttgcataa 360
 acagaaatwr ggtagtatat tgaarnacag catcattaaa rmgttwtkt wttctccctt 420
 gcaaaaaaca tgtacngact tcccgttgag taatgccaaag ttgttttttt tatnataaaa 480
 cttgcccttc attacatgtt tnaaagtggg gtgggtgggcc aaaatattga aatgatggaa 540
 ctgactgata aagctgtaca aataagcagt gtgcctaaca agcaacacag taatgttgac 600
 atgcttaatt cacaaatgct aatttcatta taaatgtttg ctaaaatata ctttgaacta 660
 tttttctgtn ttcccagagc tgagatntta gattttatgt agtatnaagt gaaaaantac 720
 gaaaataata acattgaaga aaaananaaa aanaaaaaaa a 761

<210> 189
 <211> 482
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(482)
 <223> n = A,T,C or G

```

<400> 189
tttttttttt tttgccgatn ctactatntt attgcaggan gtgggggtgt atgcaccgca      60
caccgggggt atnagaagca agaaggaagg agggagggca cagccccttg ctgagcaaca      120
aagccgcctg ctgccttctc tgtctgtctc ctggtgcagg cacatgggga gaccttcccc      180
aaggcagggg ccaccagtcc aggggtggga atacaggggg tgggangtgt gcataagaag      240
tgataggcac agggcaccgg gtacagaccc ctcggtctct gacaggtnga tttcgaccag      300
gtcattgtgc cctgcccagg cacagcgta atctggaaaa gacagaatgc tttccttttc      360
aaatttggt ngtcatngaa ngggcanttt tccaanttng gctnngtctt ggtacncttg      420
gttcggccca gctcncgct caaaaantat tcaccnnt ccnaattgct tgcnggnccc      480
cc

```

```

<210> 190
<211> 471
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(471)
<223> n = A,T,C or G

```

```

<400> 190
tttttttttt ttttaaaaca gtttttcaca acaaaattta ttagaagaat agtggttttg      60
aaaactctcg catccagtga gaactacat acaccacatt acagctngga atgtntcca      120
aatgtctggt caaatgatac aatggaacca ttcaatctta cacatgcacg aaagaacaag      180
cgcttttgac atacaatgca caaaaaaaaa aggggggggg gaccacatgg attaaaattt      240
taagtactca tcacatacat taagacacag ttctagtcca gtcnaaaatc agaactgcnt      300
tgaaaaattt catgtatgca atccaaccaa agaacttnat tggatgatcat gantntctta      360
ctacatcnac cttgatcatt gccaggaacn aaaagttnaa ancacnngt acaaaaaanaa      420
tctgtaattn anttcaacct ccgtacngaa aaatntntt tatacactcc c              471

```

```

<210> 191
<211> 402
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(402)
<223> n = A,T,C or G

```

```

<400> 191
gaggattga aggtctgttc tastgtcggm ctgttcagcc accaactcta acaagttgct      60
gtcttcact cactgtctgt aagcttttta acccagacwg tatcttcata aatagaacaa      120
attcttcacc agtcacatct tctaggacct ttttggattc agttagtata agctcttcca      180
cttcctttgt taagacttca tctggtaaag tcttaagttt tgtagaaagg aattyaattg      240
ctcgttctct aacaatgtcc tctccttgaa gtatttggct gaacaaccca cctaaagtcc      300
ctttgtgcat ccattttaaa tatactta ataggcattgk tncactaggt taaattctgc      360
aagagtcac tgtctgcaaa agttgcgtta gtatatctgc ca              402

```

```

<210> 192
<211> 601
<212> DNA

```

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(601)

<223> n = A,T,C or G

<400> 192

gagctcggat	ccaataatct	ttgtctgagg	gcagcacaca	tatncagtgc	catggnaact	60
ggtctacccc	acatgggagc	agcatgccgt	agntatataa	ggtcattccc	tgagtcagac	120
atgcytyttt	gaytaccgtg	tgccaagtgc	tggtgattct	yaacacacyt	ccatcccgyt	180
cttttgtgga	aaaactggca	cttkctctgga	actagcarga	catcacttac	aaattcaccc	240
acgagacact	tgaaagggtg	aacaaagcga	ytcttgcat	gctttttgtc	cctccggcac	300
cagttgtcaa	tactaaccgc	ctggtttgcc	tccatcacat	ttgtgatctg	tagctctgga	360
tacatctcct	gacagtactg	aagaacttct	tcttttgttt	caaaagcarc	tcttggtgcc	420
tgttggatca	ggttcccat	tcccagtcyg	aatgttcaca	tggcatattt	wacttcccac	480
aaaacattgc	gatttgaggc	tcagcaacag	caaatcctgt	tccggcattg	gctgcaagag	540
cctcgatgta	gccggccagc	gccaaaggcag	gcgccgtgag	ccccaccagc	agcagaagca	600
g						601

<210> 193

<211> 608

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(608)

<223> n = A,T,C or G

<400> 193

atacagccca	natcccacca	cgaagatgcg	cttggttgact	gagaacctga	tgccggtcact	60
ggtcccgctg	tagccccagc	gactctccac	ctgctggaag	cggttgatgc	tgcaactcytt	120
cccaacgcag	gcagmagcgg	gsccgggtcaa	tgaactccay	tcgtggcttg	gggtkgacgg	180
tkaagtgcag	gaagaggctg	accacctcgc	ggtccaccag	gatgcccag	tgtgcgggac	240
ctgcagcgaa	actcctcgat	ggatcatgagc	gggaagcgaa	tgaggcccag	ggccttgccc	300
agaaccttcc	gcctgttctc	tggcgtcacc	tgcagctgct	gccgctgaca	ctcggcctcg	360
gaccagcgga	caaacggcrt	tgaacagccg	cacctcacgg	atgcccagtg	tgctgcgctc	420
caggammgsc	accagcgtgt	ccagggtcaat	gtcgggtgaag	ccctccgcgg	gtrattggcgt	480
ctgcagtgtt	tttgtcgatg	ttctccaggc	acaggctggc	cagctgcggg	tcacgaaga	540
gtcgcgcctg	cgtgagcagc	atgaaggcgt	tgtcggctcg	cagttcttct	tcaggaactc	600
cacgcaat						608

<210> 194

<211> 392

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(392)

<223> n = A,T,C or G

<400> 194


```

gaacggctgg accttgccct gcattgtgct tgctggcagg gaataccttg gcaagcagyt      60
ccagtcagag cagccccaga ccgctgccgc ccgaagctaa gcctgcctct ggccttcccc      120
tccgcctcaa tgcagaacca gtagtgggag cactgtgttt agagttaaga gtgaacactg      180
tttgatttta cttgggaatt tcctctgtta tatagctttt cccaatgcta atttccaaac      240
aacaacaaca aaataacatg tttgcctgtt aagttgtata aaagtaggtg attctgtatt      300
taaagaaaat attactgtta catatactgc ttgcaatttc tgtatttatt gktnctstgg      360
aaataaatat agttattaaa ggttgtcant cc                                     392

```

```

<210> 195
<211> 502
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(502)
<223> n = A,T,C or G

```

```

<400> 195
ccsttkgagg ggtkaggkyc cagttyccga gtggaagaaa caggccagga gaagtgcgtg      60
ccgagctgag gcagatgttc ccacagtgc cccagagacc stgggstata gtytctgacc      120
cctcncaagg aaagaccacs ttctggggac atgggctgga gggcaggacc tagaggcacc      180
aagggaaagg cccattccgg ggstgttccc cgaggaggaa gggaaagggc tctgtgtgcc      240
ccccasgagg aagaggccct gagtcctggg atcagacacc ctttcacgtg tatccccaca      300
caaatgcaag ctcaccaagg tccccctctc gtcccccttc stacaccctg amcgccact      360
gscscacacc caccagagc acgccacccg ccatggggar tgtgctcaag gartcgcnng      420
gcarcgtgga catctngtcc cagaaggggg cagaatctcc aatagangga ctgarcmsst      480
gctnanaaaa aaaaaanaaaa aa                                     502

```

```

<210> 196
<211> 665
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(665)
<223> n = A,T,C or G

```

```

<400> 196
ggttacttgg tttcattgcc accacttagt ggatgtcatt tagaaccatt ttgtctgctc      60
cctctggaag ccttgccgag agcggaacttt gtaattgttg gagaataact gctgaatttt      120
wagctgtttk gagttgatts gcaccactgc acccacaact tcaatatgaa aacyawttga      180
actwatttat tatcttgtga aaagtataac aatgaaaatt ttgttcatac tgtattkac      240
aagtatgatg aaaagcaawa gatataatatt cttttattat gttaaattat gattgccatt      300
attaatcggc aaaatgtgga gtgtatgttc ttttcacagt aatatatgcc ttttgaact      360
tcacttgggt attttattgt aaatgartta caaaattctt aatttaagar aatggatgt      420
watatttatt tcattaattt ctttcctkgt ttacgtwaat tttgaaaaga wtgcatgatt      480
tcttgacaga aatcgatctt gatgctgtgg aagtagtttg acccacatcc ctatgagttt      540
ttcttagaat gtataaagggt tgtagcccat cnaacttcaa agaaaaaaat gaccacatac      600
tttgcaatca ggctgaaatg tggcatgctn ttctaattcc aactttataa actagcaaan      660
aagtg                                             665

```

```

<210> 197

```

```

<400> 199
agtgacttgt cctccaacaa aacccttga tcaagtttgt ggcactgaca atcagacctt      60
tgctagttcc tgtcatatat tcgtactaa atgcagactg gaggggacca aaaaggggca      120
tcaactccag ctggattatt ttggagcctg caaatctatt cctacttgta cggactttga      180

```

```

agtgattcag tttcctctac ggatgagaga ctggctcaag aatatcctca tgcagcttta 240
tgaagccnac tctgaacacg ctggttatct nagatgagaa ncagagaaat aaagtcnaga 300
aaatttacct ggangaaaag aggctttngg ctggggacca tccattgaa cttctcttta 360
anggacttta agaanaaact accacatgtn tgtngtatcc tggtgccngg ccgtttantg 420
aacntngacn ncacccttnt ggaatanant cttgaacngn tcctgaactt gtcctctgcg 480
ga 482

```

```

<210> 200
<211> 270
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1) ... (270)
<223> n = A,T,C or G

```

```

<400> 200
cggccgcaag tgcaactcca gctggggccg tgcggacgaa gattctgcca gcagttggtc 60
cgactgcgac gacggcggcg gcgacagtcg caggtgcagc gcgggcgcct ggggtcttgc 120
aaggctgagc tgacgcgcga gaggtcgtgt cacgtccacg gaccttgacg ccgtcgggga 180
cagccggaac agagcccggg gaangcggga ggcctcgggg agcccctcgg gaagggcggc 240
ccgagagata cgcaggtgca ggtggcgcgc 270

```

```

<210> 201
<211> 419
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1) ... (419)
<223> n = A,T,C or G

```

```

<400> 201
tttttttttt ttttggatc tactgcgagc acagcaggtc agcaacaagt ttattttgca 60
gctagcaagg taacagggtg gggcatggtt acatgttcag gtcaacttcc tttgtcgtgg 120
ttgattggtt tgtctttatg ggggcggggg ggggtagggg aaancgaagc anaantaaca 180
tgagtggttg gcacctccc tgtagaacct gggtacnaaa gcttggggca gttcacctgg 240
tctgtgaccg tcattttctt gacatcaatg ttattagaag tcaggatata ttttagagag 300
tccactgtnt ctggagggag attaggggtt cttgccanaa tccaancaa atccacntga 360
aaaagttgga tgatncangt acngaatacc ganggcatan ttctcatant cggtggcca 419

```

```

<210> 202
<211> 509
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1) ... (509)
<223> n = A,T,C or G

```

```

<400> 202

```

```
<210> 203
<211> 583
<212> DNA
<213> Homo sapien
```

<400> 203

```
<210> 204
<211> 589
<212> DNA
<213> Homo sapien
```

<400> 204

ttttttttct	tttttttttt	tttttttctc	ttcttttttt	ttganaatga	ggatcgagtt	60
tttcaacttc	tagatagggc	atgaagaaaa	ctcatctttc	cagcttttaa	ataacaatca	120
aatctcttat	gctatatcat	atttttaagtt	aaactaatga	gtcactggct	tatctttctcc	180
tgaaggaaat	ctgttcattc	ttctcattca	tatagttata	tcaagtacta	ccttgcatat	240
tgagagggtt	ttctttctcta	tttacacata	tatttccatg	tgaatttgta	tcaaacccttt	300
attttcatgc	aaactagaaa	ataatgtntt	cttttgcata	agagaagaga	acaatatnag	360
cattacaaaa	ctgctcaaat	tgtttgttaa	gnttatccat	tataattagt	tnggcaggag	420
ctaatacaaa	tcacattttac	ngacnagcaa	taataaaaact	gaagtaccag	ttaaatatcc	480
aaaataatta	aaggaacatt	tttagcctgg	gtataattag	ctaatttcact	ttacaagcat	540
ttatttnagaa	tgaattcaca	tgttattatt	cntagccca	acacaatgg		589

<210> 205
 <211> 545
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(545)
 <223> n = A,T,C or G

<400> 205
 tttttntttt ttttttcagt aataatcaga acaatattta tttttatatt taaaattcat 60
 agaaaagtgc cttacattta ataaaagttt gtttctcaaa gtgatcagag gaattagata 120
 tngtcttgaa caccaatatt aatttgagga aaatacacca aaatacatta agtaaattat 180
 ttaagatcat agagcttgta agtgaaaaga taaaatttga cctcagaaac tctgagcatt 240
 aaaaatccac tattagcaaa taaattacta tggacttctt gctttaattt tgtgatgaat 300
 atggggtgtc actggtaaac caacacattc tgaaggatac attacttagt gatagattct 360
 tatgtacttt gctanatnac gtggatatga gttgacaagt ttctctttct tcaatctttt 420
 aaggggcnga ngaaatgagg aagaaaagaa aaggattacg catactgttc tttctatngg 480
 aaggattaga tatgtttcct ttgccaatat taaaaaata ataatgttta ctactagtga 540
 aaccc 545

<210> 206
 <211> 487
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(487)
 <223> n = A,T,C or G

<400> 206
 tttttttttt ttttttagtc aagtttctna tttttattat aattaaagtc ttggtcattt 60
 catttattag ctctgcaact tacatattta aattaaagaa acgttnttag acaactgtna 120
 caatttataa atgtaagggtg ccattattga gtanatatat tcctccaaga gtggatgtgt 180
 cccttctccc accaactaat gaancagcaa cattagttta attttattag tagatnatac 240
 actgctgcaa acgctaattc tcttctccat ccccatgtng atattgtgta tatgtgtgag 300
 ttggtagnaa tgcatcanca atctnacaat caacagcaag atgaagctag gcntgggctt 360
 tcggtgaaaa tagactgtgt ctgtctgaat caaatgatct gacctatcct cgggtggcaag 420
 aactcttoga accgcttcct caaaggcngc tgccacattt gtggcntctn ttgcacttgt 480
 ttcaaaa 487

<210> 207
 <211> 332
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(332)
 <223> n = A,T,C or G

<400> 207

```

tgaattggct aaaagactgc atttttanaa ctagcaactc ttattttcttt ccttttaaaaa      60
tacatagcat taaatcccaa atcctattta aagacctgac agcttgagaa ggctcactact      120
gcatttatag gaccttctgg tggttctgct gttacntttg aantctgaca atccttgana      180
atctttgcat gcagaggagg taaaaggtat tggattttca cagaggaana acacagcgca      240
gaaatgaagg ggccaggctt actgagcttg tccactggag ggctcatggg tgggacatgg      300
aaaagaaggc agcctaggcc ctggggagcc ca                                     332

```

```

<210> 208
<211> 524
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(524)
<223> n = A,T,C or G

```

```

<400> 208
agggcggtggt gcgaggggcg ttactgtttt gtctcagtaa caataaatac aaaaagactg      60
gttgtgttcc ggcccatcc aaccacgaag ttgatttctc ttgtgtgcag agtgactgat      120
tttaaaggac atggagcttg tcacaatgtc acaatgtcac agtgtgaagg gcacactcac      180
tcccgctgga ttcacattta gcaaccaaca atagctcatg agtccatact tgtaaatact      240
tttggcagaa tacttnttga aacttgacaga tgataactaa gatccaagat atttcccaaa      300
gtaaatagaa gtgggtcata atattaatta cctgttcaca tcagcttcca ttacaagtc      360
atgagcccag aactgacat caaactaagc ccacttagac tcctcaccac cagtctgtcc      420
tgtcatcaga caggaggctg tcaccttgac caaattctca ccagtcaatc atctatccaa      480
aaaccattac ctgatccact tccggtaatg caccaccttg gtga                                     524

```

```

<210> 209
<211> 159
<212> DNA
<213> Homo sapien

```

```

<400> 209
gggtgaggaa atccagagtt gccatggaga aaattccagt gtcagcattc ttgctccttg      60
tggcctctc ctacactctg gccagagata ccacagtcaa acctggagcc aaaaaggaca      120
caaaggactc tcgaccctaa ctgccccaga ccctctcca                                     159

```

```

<210> 210
<211> 256
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(256)
<223> n = A,T,C or G

```

```

<400> 210
actccctggc agacaaaggc agaggagaga gctctgttag ttctgtgttg ttgaactgcc      60
actgaatttc ttccacttg gactattaca tgccanttga gggactaatg gaaaaacgta      120
tggggagatt ttanccaatt tangtntgta aatggggaga ctggggcagg cgggagagat      180
ttgcagggtg naaatgggan ggctggtttg ttanatgaac agggacatag gaggtaggca      240
ccaggatgct aaatca                                     256

```

<210> 211
 <211> 264
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(264)
 <223> n = A,T,C or G

<400> 211
 acattgtttt tttagataa agcattgaga gagctctcct taacgtgaca caatggaagg 60
 actggaacac ataccacat ctttgttctg agggataatt ttctgataaa gtcttgctgt 120
 atattcaagc acatatgtta tatattattc agttccatgt ttatagccta gttaaggaga 180
 ggggagatac attcngaaag aggactgaaa gaaatactca agtnggaaaa cagaaaaaga 240
 aaaaaaggag caaatgagaa gcct 264

<210> 212
 <211> 328
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(328)
 <223> n = A,T,C or G

<400> 212
 acccaaaaaat ccaatgctga atatttggtc tcattattcc canattcttt gattgtcaaa 60
 ggattttaatg ttgtctcagc ttgggcactt cagttaggac ctaaggatgc cagccggcag 120
 gtttatatat gcagcaacaa tattcaagcg cgacaacagg ttattgaact tgcccggcag 180
 ttnaatttca ttccattga cttgggatcc ttatcatcag ccagagagat tgaaaattta 240
 ccctacnac tctttactct ctgganaggg ccagtgggtg tagctataag cttggccaca 300
 tttttttttc ctttattcct ttgtcaga 328

<210> 213
 <211> 250
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(250)
 <223> n = A,T,C or G

<400> 213
 acttatgagc agagcgacat atccnagtgt agactgaata aaactgaatt ctctccagtt 60
 taaagcattg ctactgaag ggatagaagt gactgccagg agggaaagta agccaaggct 120
 cattatgcca aagganatat acatttcaat tctccaaaact tcttctcat tccaagagtt 180
 ttcaatattt gcatgaacct gctgataanc catgttaana aacaaatatc tctctnacct 240
 tctcatcggt 250

<210> 214

006230 "SCTG60"

<211> 444
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(444)
 <223> n = A,T,C or G

<400> 214
 acccagaatc caatgctgaa tatttggtc cattattccc agattctttg attgtcaaag 60
 gatttaaatg tgtctcagct tgggcacttc agttaggacc taaggatgcc agccggcagg 120
 tttatatatg cagcaacaat attcaagcgc gacaacaggc tattgaactt gcccgccagt 180
 tgaatttcac tcccattgac ttgggaccc tatcatcagc canagagatt gaaaatttac 240
 ccctacgact ctttactctc tggagagggc cagtgggtgg agctataagc ttggccacat 300
 ttttttttcc tttattccct tgtcagagat gcgattcatc catatgctan aaaccaacag 360
 agtgactttt acaaaattcc tataganatt gtgaataaaa cttacctat agttgccatt 420
 actttgctct ccctaataata cctc 444

<210> 215
 <211> 366
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(366)
 <223> n = A,T,C or G

<400> 215
 acttatgagc agagcgacat atccaagtgt anactgaata aaactgaatt ctctccagtt 60
 taaagcattg ctactgaag ggatagaagt gactgccagg agggaaagta agccaaggct 120
 cattatgcca aagganatat acatttcaat tctccaaact tcttcctcat tccaagagtt 180
 ttcaatattt gcatgaacct gctgataagc catgttgaga aacaaatata tctctgacct 240
 tctcatcggt aagcagaggc tgtaggcaac atggaccata gcgaanaaaa aacttagtaa 300
 tccaagctgt tttctacact gtaaccaggt ttccaaccaa ggtggaaatc tcctatactt 360
 ggtgcc 366

<210> 216
 <211> 260
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(260)
 <223> n = A,T,C or G

<400> 216
 ctgtataaac agaactccac tgcangaggg agggccgggc caggagaatc tccgcttgct 60
 caagacaggg gcctaaggag ggtctccaca ctgctnntaa gggctnttnc atttttttat 120
 taataaaaag tnnaaaaggc ctcttctcaa cttttttccc ttnggctgga aaatttaaaa 180
 atcaaaaatt tcctnaagtt ntcaagctat catatatact ntatcctgaa aaagcaacat 240
 aattcttctt tccctccttt 260

006230"3E2T560

<210> 221
<211> 167

<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(167)
<223> n = A,T,C or G

<400> 221
actangtgca ggtgcgcaca aatatttgtc gatattccct tcattcttga ttccatgagg 60
tcttttgcgc agcctgtggc tctactgtag taagtttctg ctgatgagga gccagnatgc 120
ccccactac cttccctgac gctccccana aatcacccaa cctctgt 167

<210> 222
<211> 351
<212> DNA
<213> Homo sapien

<400> 222
agggcgtggt gcggaggcgc gtactgacct cattagtagg aggatgcatt ctggcacccc 60
gttcttcacc tgtcccccaa tctttaaag gccatactgc ataaagtcaa caacagataa 120
atgtttgctg aattaaagga tggatgaaaa aaattaataa tgaatttttg cataatccaa 180
ttttctcttt tatatttcta gaagaagttt ctttgagcct attagatccc gggaatcttt 240
taggtgagca tgattagaga gctttaggtg tgcttttaca tatatctggc atatttgagt 300
ctcgtatcaa aacaatagat tggtaaaggt ggtattattg tattgataag t 351

<210> 223
<211> 383
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(383)
<223> n = A,T,C or G

<400> 223
aaaacaaaca acaaaaaaaaa acaattcttc attcagaaaa attatcttag ggactgatat 60
tggttaattat ggtcaattta atwrtrttkt ggggcatttc cttacattgt cttgacaaga 120
ttaaaatgtc tgtgccaaaa ttttgtattt tatttgagga cttcttatca aaagtaatgc 180
tgccaaagga agtctaagga attagtagtg ttcccmtcac ttgtttggag tgtgctattc 240
taaaagattt tgatttcctg gaatgacaat tatattttta ctttggtggg ggaaanagtt 300
ataggaccac agtcttcact tctgatactt gttaaattaat cttttattgc acttgttttg 360
accattaagc tatatgttta aaa 383

<210> 224
<211> 320
<212> DNA
<213> Homo sapien

<400> 224
cccctgaagg cttcttggtta gaaaatagta cagttacaac caataggaac acaaaaaaga 60
aaaagtttgt gacattgtag tagggagtgt gtacccttca ctcccatca aaaaaaaaaat 120
ggatacatgg ttaaaggata raagggaat attttatcat atgttctaaa agagaaggaa 180

006230"325960

```
<210> 225
<211> 1214
<212> DNA
<213> Homo sapien
```

```
<210> 226
<211> 119
<212> DNA
<213> Homo sapien
```

```
<210> 227
<211> 818
<212> DNA
<213> Homo sapien
```

<400> 227						
acaattcata	gggacgacca	atgaggacag	ggaatgaacc	cggctctccc	ccagccctga	60
tttttgctac	atatggggtc	ccttttccatt	ctttgcaaaa	acactgggtt	ttctgagaac	120
acggacggtt	cttagcacia	tttgtgaaat	ctgtgtaraa	ccgggctttg	caggggagat	180
aattttcctc	ctctggagga	aaggtggtga	ttgacaggca	gggagacagt	gacaaggcta	240
gaaaaagcca	cgctcggcct	tctctgaacc	aggatggaac	ggcagacccc	tgaaaacgaa	300
gcttgctccc	ttccaatcag	ccacttctga	gaacccccat	ctaacttcct	actggaaaag	360
agggcctcct	caggagcagt	ccaagagttt	tcaaagataa	cgtgacaact	accatctaga	420

ggaaaggggtg	caccctcagc	agagaagccg	agagcttaac	tctggtcggt	tccagagaca	480
acctgctggc	tgtcttgga	tgcgccagc	ctttgagagg	ccactacccc	atgaacttct	540
gccatccact	ggacatgaag	ctgaggacac	tgggcttcaa	cactgagttg	tcatgagagg	600
gacaggctct	gccctcaagc	cggctgaggg	cagcaaccac	tctcctcccc	tttctcacgc	660
aaagccattc	ccacaaatcc	agaccatacc	atgaagcaac	gagacccaaa	cagtttggt	720
caagaggata	tgaggactgt	ctcagcctgg	ctttgggctg	acaccatgca	cacacacaag	780
gtccacttct	agggttttcag	cctagatggg	agtcgtgt			818

<210> 228
 <211> 744
 <212> DNA
 <213> Homo sapien

<400> 228						
actggagaca	ctgttgaact	tgatcaagac	ccagaccacc	ccaggtctcc	ttcgtgggat	60
gtcatgacgt	ttgacatacc	tttggaaacga	gcctcctcct	tggaagatgg	aagaccgtgt	120
tctggccga	cctggcctct	cctggcctgt	ttcttaagat	gcggagtcac	atttcaatgg	180
taggaaaagt	ggcttcgtaa	aatagaagag	cagtcactgt	ggaactacca	aatggcgaga	240
tgctcggtgc	acattgggggt	gctttgggat	aaaagattta	tgagccaact	attctctggc	300
accagattct	aggccagttt	gttccactga	agcttttccc	acagcagtcc	acctctgcag	360
gctggcagct	gaatggcttg	ccgggtggctc	tgtggcaaga	tcacactgag	atcgatgggt	420
gagaaggcta	ggatgcttgt	ctagtgttct	tagctgtcac	gttggctcct	tccaggttgg	480
ccagacgggtg	ttggccactc	cctttctaaaa	cacaggcgcc	ctcctgggtga	cagtgacccg	540
ccgtgggtatg	ccttggccca	ttccagcagt	cccagttatg	catttcaagt	ttggggtttg	600
ttcttttctg	taatgttcc	ctgtgttgtc	agctgtcttc	atttctggg	ctaagcagca	660
ttgggagatg	tggaccagag	atccactcct	taagaaccag	tggcgaaaga	cactttcttt	720
cttactctg	aagtagctgg	tggt				744

<210> 229
 <211> 300
 <212> DNA
 <213> Homo sapien

<400> 229						
cgagtctggg	ttttgtctat	aaagtttgat	ccctcctttt	ctcatccaaa	tcatgtgaac	60
cattacacat	cgaaataaaa	gaaaggtggc	agacttgccc	aacgccaggc	tgacatgtgc	120
tgcagggttg	ttgtttttta	attattattg	ttagaaacgt	caccacagc	ccctgttaat	180
ttgtatgtga	cagccaactc	tgagaaggtc	ctatttttcc	acctgcagag	gatccagtct	240
cactaggctc	ctccttgccc	tcacactgga	gtctccgcca	gtgtgggtgc	ccactgacat	300

<210> 230
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 230						
cagcagaaca	aatacaaata	tgaagagtgc	aaagatctca	taaaatctat	gctgaggaat	60
gagcgacagt	tcaaggagga	gaagcttgca	gagcagctca	agcaagctga	ggagctcagg	120
caatataaag	tcttggttca	cactcaggaa	cgagagctga	cccagttaag	ggagaagttg	180
cgggaaggga	gagatgcctc	cctctcattg	aatgagcatc	tccaggccct	cctcactccg	240
gatgaaccgg	acaagtccca	ggggcaggac	ctccaagaaa	cagacctcgg	ccgcgaccac	300
g						301

<210> 231

<211> 301
 <212> DNA
 <213> Homo sapien

<400> 231
 gcaagcacgc tggcaaactct ctgtcaggtc agctccagag aagccattag tcatttttagc 60
 caggaactcc aagtccacat ccttggaac tggggacttg cgcaggtag ccttgaggat 120
 ggcaacacgg gactttctcat caggaagtgg gatgtagatg agctgatcaa gacggccagg 180
 tctgaggatg gcaggatcaa tgatgtcagg ccggttggtg ccgccaatga tgaacacatt 240
 tttttttgtg gacatgccat ccatttctgt caggatctgg ttgatgactc ggtcagcagc 300
 c 301

<210> 232
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 232
 agtaggtatt tcgtgagaag ttcaacacca aaactggaac atagttctcc ttcaagtgtt 60
 ggcgacagcg gggcttctctg attctggaat ataactttgt gtaaattaac agccacctat 120
 agaagagtcc atctgctgtg aaggagagac agagaactct gggttccgtc gtcctgtcca 180
 cgtgctgtac caagtgtctg tgccagcctg ttacctgttc tactgaaaa tctggctaatt 240
 gctcttgtgt atcacttctg attctgacaa tcaatcaatc aatggcctag agcactgact 300
 g 301

<210> 233
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 233
 atgactgact tcccagtaag gctctctaag gggtaagtag gaggatccac aggatttgag 60
 atgctaaggc cccagagatc gtttgatcca accctcttat tttcagaggg gaaaatgggg 120
 cctagaagtt acagagcatc tagctggtgc gctggcacc cttggcctcac acagactccc 180
 gagtagctgg gactacaggc acacagtcac tgaagcaggc cctgttagca attctatgcg 240
 tacaaattaa catgagatga gtagagactt tattgagaaa gcaagagaaa atcctatcaa 300
 c 301

<210> 234
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 234
 aggtcctaca catcgagact catccatgat tgatatgaat ttaaaaatta caagcaaaga 60
 cattttattc atcatgatgc tttcttttgt ttcttctttt cgttttcttc tttttctttt 120
 tcaatttcag caacatactt ctcaatttct tcaggattta aaatcttgag ggattgatct 180
 cgcctcatga cagcaagttc aatgtttttg ccacctgact gaaccacttc caggagtgcc 240
 ttgatcacca gcttaatggg cagatcatct gcttcaatgg cttcgtcagt atagttcttc 300
 t 301

<210> 235
 <211> 283
 <212> DNA

<213> Homo sapien

<400> 235

tggggctgtg	catcaggcgg	gtttgagaaa	tattcaattc	tcagcagaag	ccagaatttg	60
aattccctca	tcttttaggg	aatcatttac	caggtttgga	gaggattcag	acagctcagg	120
tgctttcact	aatgtctctg	aactttctgtc	cctctttgtt	catggatagt	ccaataaata	180
atgttatctt	tgaactgatg	ctcataggag	agaatataag	aactctgagt	gatatcaaca	240
ttagggattc	aaagaaatat	tagatttaag	ctcacactgg	tca		283

<210> 236

<211> 301

<212> DNA

<213> Homo sapien

<400> 236

aggtcctcca	ccaactgcct	gaagcacggg	taaaattggg	aagaagtata	gtgcagcata	60
aatactttta	aatcgatcag	atttccctaa	cccacatgca	atcttcttca	ccagaagagg	120
tcggagcagc	atcattaata	ccaagcagaa	tgcgtaatag	ataaatacaa	tggtatatag	180
tgggtagacg	gcttcatgag	tacagtgtac	tgtgggtatcg	taatctggac	ttgggttgta	240
aagcatcgtg	taccagtcag	aaagcatcaa	tactcgacat	gaacgaatat	aaagaacacc	300
a						301

<210> 237

<211> 301

<212> DNA

<213> Homo sapien

<400> 237

cagtggtagt	ggtgggtggac	gtggcggttg	togtgggtgcc	ttttttggtg	cccgtcacaa	60
actcaatttt	tgttcgctcc	tttttggcct	tttccaattt	gtccatctca	attttctggg	120
ccttggctaa	tgcctcatag	taggagtcct	cagaccagcc	atggggatca	aacatatact	180
ttgggtagtt	ggtgccaaagc	togtcaatgg	cacagaatgg	atcagcttct	cgtaaatacta	240
gggttccgaa	attcttttctt	ccttttgata	atgtagttca	tatccattcc	ctcctttatc	300
t						301

<210> 238

<211> 301

<212> DNA

<213> Homo sapien

<400> 238

gggcagggtt	tttttttttt	ttttttgatg	gtgcagaccc	ttgctttatt	tgtctgactt	60
gttcacagtt	cagccccctg	ctcagaaaac	caacggggcca	gctaaggaga	ggaggaggca	120
ccttgagact	tccggagtcg	aggctctcca	gggttcccca	gcccataaat	cattttctgc	180
acccccctgc	tgggaagcag	ctccctgggg	ggtgggaatg	ggtgactaga	agggatttca	240
gtgtgggacc	cagggtctgt	tcttcacagt	aggaggtgga	agggatgact	aattttctta	300
t						301

<210> 239

<211> 239

<212> DNA

<213> Homo sapien

<400> 239

```
<210> 240
<211> 300
<212> DNA
<213> Homo sapien
```

```
<210> 241
<211> 301
<212> DNA
<213> Homo sapien
```

```
<210> 242
<211> 301
<212> DNA
<213> Homo sapien
```

```
<210> 243
<211> 301
<212> DNA
<213> Homo sapien
```

<400>	243					
aggtaagtcc	cagtttgaag	ctcaaaagat	ctggtatgag	cataggctca	tgcagacat	60
ggtggcccaa	gctatgaaat	cagagggagg	cttcattctg	gctgtaaaa	actatgatgg	120
tgacgtgcag	tggactctg	tggcccaagg	gtatggctct	ctcggcatga	tgaccagcgt	180
gctggtttgt	ccagatggca	agacagtaga	agcagaggct	gccacgggga	ctgtaacccg	240
tcactaccgc	atgttccaga	aaggacagga	gacgtccacc	aatcccattg	cttccatttt	300

t

301

<210> 244
 <211> 300
 <212> DNA
 <213> Homo sapien

<400> 244
 gctggtttgc aagaatgaaa tgaatgattc tacagctagg acttaacctt gaaatggaaa 60
 gtcattgcaat cccatttgca ggatctgtct gtgcacatgc ctctgtagag agcagcattc 120
 ccaggacact tggaacacagt tgacactgta aggtgcttgc tcccccaagac acatcctaaa 180
 aggtgttgta atggtgaaaa cgtcttcctt ctttattgcc ccttcttatt tatgtgaaca 240
 actggtttgtc ttttgtgtat cttttttaaa ctgtaaagtt caattgtgaa aatgaatatc 300

<210> 245
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 245
 gtctgagtat ttaaaatggt attgaaatta tccccaacca atgttagaaa agaaagaggt 60
 tatatactta gataaaaaat gaggtgaatt actatccatt gaaatcatgc tcttagaatt 120
 aaggccagga gatattgtca ttaatgtara cttcaggaca ctagagtata gcagccctat 180
 gttttcaaaag agcagagatg caattaaata ttgttttagca tcaaaaaggc cactcaatac 240
 agctaataaa atgaaagacc taattttctaa agcaattctt tataattttac aaagttttta 300
 g 301

<210> 246
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 246
 ggtctgtcct acaatgcctg cttcttgaaa gaagtcggca ctttctagaa tagctaaata 60
 acctgggctt attttaaaga actatttgta gctcagattg gttttcctat ggctaaaata 120
 agtgcttctt gtgaaaatta aataaaacag ttaattcaaa gccttgatat atgttaccac 180
 taacaatcat actaaatata ttttgaagta caaagtttga catgctctaa agtgacaacc 240
 caaatgtgtc ttacaaaaca cgttcctaac aagggtatgct ttacactacc aatgcagaaa 300
 c 301

<210> 247
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 247
 aggtcctttg gcagggtcga tggatcagag ctcaaactgg agggaaaggc atttcgggta 60
 gcctaagagg gcgactggcg gcagcacaac caaggaaggc aagggtgttt cccccacgct 120
 gtgtcctgtg ttcagggtcg acacacaatc ctcatgggaa caggatcacc catgcgctgc 180
 ccttgatgat caagggttggg gcttaagtgg attaaggagg gcaagttctg ggttccttgc 240
 cttttcaaac catgaagtca ggctctgtat ccctcctttt cctaactgat attctaacta 300
 a 301

<210> 248

<211> 301
 <212> DNA
 <213> Homo sapien

<400> 248
 aggtccttgg agatgccatt tcagccgaag gactcttctw ttcggaagta caccctcact 60
 attaggaaga ttcttagggg taatttttct gaggaaggag aactagccaa cttaagaatt 120
 acaggaagaa agtgggttgg aagacagcca aagaaataaa agcagattaa attgtatcag 180
 gtacattcca gcctgttggc aactccataa aaacatttca gattttaatc ccgaatttag 240
 ctaatgagac tggatttttg ttttttatgt tgtgtgtcgc agagctaaaa actcagttcc 300
 c 301

<210> 249
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 249
 gtccagagga agcacctggg gctgaactag gcttgccctg ctgtgaactt gcacttggag 60
 ccctgacgct gctgttctcc ccgaaaaacc cgaccgacct ccgcgatctc cgtcccgcgc 120
 ccaggagac acagcagtga ctacagagctg gtcgcacact gtgcctccct cctcaccgcc 180
 catcgtaatg aattattttg aaaattaatt ccaccatcct ttcagattct ggatggaaag 240
 actgaatctt tgactcagaa ttgtttgctg aaaagaatga tgtgactttc ttagtcattt 300
 a 301

<210> 250
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 250
 ggtctgtgac aaggacttgc aggctgtggg aggcaagtga cccttaacac tacatttctc 60
 cttatcttta ttggcttgat aaacataatt atttctaaca ctagcttatt tccagttgcc 120
 cataagcaca tcagtacttt tctctggctg gaatagtaaa ctaaagtatg gtacatctac 180
 ctaaaagact actatgtgga ataatacata ctaatgaagt attacatgat ttaaagacta 240
 caataaaacc aaacatgctt ataacattaa gaaaaacaat aaagatacat gattgaaacc 300
 a 301

<210> 251
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 251
 gccgaggtcc tacatttggc ccagtttccc cctgcctcct ctccagggcc cctgcctcat 60
 agacaacctc atagagcata ggagaactgg ttgccctggg ggcaggggga ctgtctggat 120
 ggcagggggtc ctcaaaaatg ccactgtcac tgccaggaaa tgcttctgag cagtacacct 180
 cattggggtc aatgaaaagc ttcaagaaat cttcaggctc actctcttga aggccgggaa 240
 cctctggagg ggggcagtgg aatcccagct ccaggacgga tcctgtcgaa aagatatcct 300
 c 301

<210> 252
 <211> 301
 <212> DNA

006230 "366T560

<400> 252

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<210> 253
<211> 301
<212> DNA
<213> Homo sapien
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<400> 253

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<210> 254
<211> 301
<212> DNA
<213> Homo sapien
```

<400> 254

```
<210> 255
<211> 302
<212> DNA
<213> Homo sapien
```

<400> 255

```
<210> 256
<211> 301
<212> DNA
<213> Homo sapien
```

<220>
 <221> misc_feature
 <222> (1)...(301)
 <223> n = A,T,C or G

<400> 256
 gttccagaaa acattgaagg tggcttccca aagtctaact agggataccc cctctagcct 60
 aggaccctcc tccccacacc tcaatccacc aaaccatcca taatgcaccc agataggccc 120
 acccccacaaa gcctggacac cttgagcaca cagttatgac caggacagac tcattctctat 180
 aggcaaatag ctgctggcaa actggcatta cctggtttgt ggggatgggg gggcaagtgt 240
 gtggcctctc ggctgggta gcaagaacat tcagggtagg cctaagttan tcgtgttagt 300
 t 301

<210> 257
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 257
 gttgtggagg aactctggct tgctcattaa gtcctactga ttttcactat cccctgaatt 60
 tccccactta tttttgtctt tcactatcgc aggccttaga agaggtctac ctgcctccag 120
 tcttacctag tccagtctac cccctggagt tagaatggcc atcctgaagt gaaaagtaat 180
 gtcacattac tcccttcagt gatctcttgt agaagtgcc atccctgaat gccaccaaga 240
 tcttaattctt cacatcttta atcttatctc ttgtactcct ctttacaccg gagaaggctc 300
 c 301

<210> 258
 <211> 301
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(301)
 <223> n = A,T,C or G

<400> 258
 cagcagtagt agatgccgta tgccagcacg cccagcactc ccaggatcag caccagcacc 60
 aggggcccag ccaccaggcg cagaagcaag ataaacagta ggctcaagac cagagccacc 120
 cccagggcaa caagaatcca ataccaggac tgggcaaaat cttcaaagat ctttaacctg 180
 atgtctcggg cattgaggct gtcaataana cgctgatccc ctgctgtatg gtggtgtcat 240
 tgggtgatccc tgggagcgcc ggtggagtaa cgtttgtcca tggaaagcag cgcccacaac 300
 t 301

<210> 259
 <211> 301
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(301)
 <223> n = A,T,C or G

005230 = 364590

<400> 259
 tcatatatgc aaacaaatgc agactangcc tcaggcagag actaaaggac atctcttggg 60
 gtgtcctgaa gtgatttgga cccctgaggg cagacaccta agtaggaatc ccagtgggaa 120
 gcaaagccat aaggaagccc aggattcctt gtgatcagga agtgggccag gaaggctctgt 180
 tccagctcac atctcatctg catgcagcac ggaccggatg cggccactgg gtcttggctt 240
 cccctcccatc ttctcaagca gtgtccttgt tgagccattt gcaccccttg ctccagggtg 300
 c 301

<210> 260
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 260
 ttttttttct ccctaaggaa aaagaaggaa caagtctcat aaaaccaa at aagcaatggt 60
 aagggtgtctt aacttgaaaa agattaggag tctctgggtt acaagttata attgaatgaa 120
 agaactgtaa cagccacagt tggccatttc atgccaatgg cagcaaacia caggattaac 180
 tagggcaaaa taaataagtg tgtggaagcc ctgataagtg cttaataaac agactgattc 240
 actgagacat cagtacctgc ccgggcggcc gctcgagccg aattctgcag atatccatca 300
 c 301

<210> 261
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 261
 aaatattcga gcaaactctg taactaatgt gtctccataa aaggctttga actcagtga 60
 tctgcttcca tccacgattc tagcaatgac ctctcggaca tcaaagctcc tcttaagggt 120
 agcaccaact attccatata attcatcagc aggaaataaa ggctcttcag aagggtcaat 180
 ggtgacatcc aattttcttct gataatttag attcctcaca accttcttag ttaagtgaag 240
 ggcatgatga tcatccaaag cccagtgggtc acttactcca gactttctgc aatgaagatc 300
 a 301

<210> 262
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 262
 gaggagagcc tggtacagca tttgtaagca cagaatactc caggagtatt tgtaattgtc 60
 tgtgagcttc ttgccgcaag tctctcagaa atttaaaaag atgcaaatac ctgagtcacc 120
 cctagacttc ctaaaccaga tcctctgggg ctggaacctg gcactctgca tttgtaatga 180
 gggctttctg gtgcacacct aattttgtgc atctttgccc taaatcctgg attagtccc 240
 catcattacc cccacattat aatgggatag attcagagca gatactctcc agcaaagaat 300
 c 301

<210> 263
 <211> 301
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature

<222> (1)...(301)
 <223> n = A,T,C or G

<400> 263
 tttagcttgt ggtaaatagac tcacaaaact gatttttaaaa tcaagttaat gtgaattttg 60
 aaaattacta ctttaataccta attcacaata acaatggcat taaggtttga cttgagttgg 120
 ttcttagtat tatttatggg aaataggctc ttaccacttg caaataactg gccacatcat 180
 taatgactga cttcccagta aggcctctcta aggggtaagt angaggatcc acaggatttg 240
 agatgctaag gccccagaga tcgtttgatc caaccctctt attttcagag gggaaaatgg 300
 g 301

<210> 264
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 264
 aaagacgtta aaccactcta ctaccacttg tggaactctc aaagggtaaa tgacaaaasc 60
 aatgaatgac tctaaaaaca atatttacat ttaatggttt gtagacaata aaaaaacaag 120
 gtggatagat ctagaattgt aacattttta gaaaaccata scatttgaca gatgagaaag 180
 ctcaattata gatgcaaagt tataactaaa ctactatagt agtaaagaaa tacatttcac 240
 acccttcata taaattcact atcttggctt gaggcactcc ataaaatgta tcacgtgcat 300
 a 301

<210> 265
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 265
 tgcccaagtt atgtgtaagt gtatccgcac ccagaggtaa aactacactg tcattcttctg 60
 cttcttctga cgcagtattt cttctctggg gagaagccgg gaagtcttct cctggctcta 120
 catattcttg gaagtctcta atcaactttt gttccatttg tttcatttct tcaggaggga 180
 ttttcagttt gtcaacatgt tctctaacaa caattgcca tttctgtaaa gaatccaaag 240
 cagtccaagg ctttgacatg tcaacaacca gcataactag agtatccttc agagatacgg 300
 c 301

<210> 266
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 266
 taccgtctgc ctttctctcc atccaggcca tctgcgaatc tacatgggtc ctctattctg 60
 acaccagatc actctttcct ctaccacag gcttgctatg agcaagagac acaacctcct 120
 ctcttctgtg ttccagcttc ttttctgtt cttcccaccc cttaagttct attcctgggg 180
 atagagacac caatacccat aacctctctc ctaagcctcc ttataaccca ggggtgcacag 240
 cacagactcc tgacaactgg taaggccaat gaactgggag ctcacagctg gctgtgcctg 300
 a 301

<210> 267
 <211> 301
 <212> DNA
 <213> Homo sapien

$\langle 220 \rangle$

<221> misc_feature
 <222> (1)...(301)
 <223> n = A,T,C or G

<400> 271
 aaaaggTtct cataagatta acaattttaa taaatatttg atagaacatt ctttctcatt 60
 tttatagctc atcttttaggg ttgatattca gttcatgctt cccttgctgt tcttgatcca 120
 gaattgcaat cacttcatca gcctgtattc gctccaattc tctataaagt gggccaagg 180
 tgaaccacag agccacagca cacctctttc ccttggtgac tgccttcacc ccatganggt 240
 tctctcctcc agatganaac tgatcatgcg cccacatttt gggttttata gaagcagtca 300
 c 301

<210> 272
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 272
 taaattgcta agccacagat aacaccaatc aaatggaaca aatcactgtc ttcaaagtgc 60
 ttatcagaaa accaaatgag cctggaatct tcataatacc taaacatgcc gtatttagga 120
 tccaataatt ccctcatgat gagcaagaaa aattctttgc gcacccctcc tgcattccaca 180
 gcatcttctc caacaaatat aaccttgagt ggcttcttgt aatctatgtt ctttgttttc 240
 ctaaggactt ccattgcatc tcctacaata ttttctctac gcaccactag aattaagcag 300
 g 301

<210> 273
 <211> 301
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(301)
 <223> n = A,T,C or G

<400> 273
 acatgtgtgt atgtgtatct ttgggaaaaa aanaagacat cttgtttayt atttttttgg 60
 agagangctg ggacatggat aatcacwtaa tttgctayta tyactttaat ctgactygaa 120
 gaaccgtcta aaaataaaaat ttaccatgtc dtatattcct tatagtatgc ttatttcacc 180
 ttytttctgt ccagagagag tatcagtgac ananatttma ggggtgaamac atgmattggt 240
 gggacttnty tttacngagm accctgcccg sgcgccctcg makcngantt ccgcsananc 300
 t 301

<210> 274
 <211> 301
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(301)
 <223> n = A,T,C or G

<400> 274

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cttatataact ctttctcaga ggcaaaagag gagatgggta atgtagacaa ttctttgagg      60
aacagtaaat gattattaga gagaangaat ggaccaagga gacagaaatt aacttgtaaa      120
tgattctctt tggaatctga atgagatcaa gaggccagct ttagcttggt gaaaagtcca      180
tctaggtatg gttgcattct cgtcttcttt tctgcagtag ataatgaggt aaccgaaggc      240
aattgtgctt cttttgataa gaagctttct tggtcatatc aggaaattcc aganaaaagtc      300
c                                                                           301

```

```

<210> 275
<211> 301
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

```

```

<400> 275
tcggtgtcag cagcacgtgg cattgaacat tgcaatgtgg agcccaaacc acagaaaatg      60
gggtgaaatt ggccaacttt ctattaactt atgttggcaa ttttgccacc aacagtaagc      120
tggcccttct aataaaagaa aattgaaagg tttctcacta aacggaatta agtagtggag      180
tcaagagact ccagggcctc agcgtaacctg cccggggcggc cgctcgaagc cgaattctgc      240
agatatccat cacactggcg gncgctcgan catgcatcta gaaggnccaa ttgcacctat      300
a                                                                           301

```

```

<210> 276
<211> 301
<212> DNA
<213> Homo sapien

```

```

<400> 276
tgtacacata ctcaataaat aaatgactgc attgtggtat tattactata ctgattatat      60
ttatcatgtg acttctaatt agaaaatgta tccaaaagca aaacagcaga tatacaaaat      120
taaagagaca gaagatagac attaacagat aaggcaactt atacattgag aatccaaatc      180
caatacattt aaacatttgg gaaatgaggg ggacaaatgg aagccagatc aaatttgtgt      240
aaaactattc agtatgttcc ccttgcttca tgtctgagaa ggctctcctt caatggggat      300
g                                                                           301

```

```

<210> 277
<211> 301
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

```

```

<400> 277
tttgttgatg tcagtatttt attacttgcg ttatgagtgc tcacctggga aattctaaag      60
atacagagga cttggaggaa gcagagcaac tgaattttaat ttaaaagaag gaaaacattg      120
gaatcatggc actcctgata ctttcccaa tcaacactct caatgcccc cctcgtcct      180
caccatagtg gggagactaa agtggccacg gatttgcctt angtgtgcag tgcgttctga      240
gttcnctgtc gattacatct gaccagtctc ctttttccga agtcnctccg ttcaatcttg      300

```


<400> 281

<210> 282

<211> 301

<212> DNA

<213> Homo sapien

<400> 282

caggtactac	agcaattaaaa	tactgacaag	caagtagttt	cttggcgtgc	acgaattgca	60
tccagaaccc	aaaaattaa	aaattcaaaa	agacattttg	tgggcacctg	ctagcacaga	120
agcgcagaag	caaagcccag	gcagaaccat	gctaacctta	cagctcagcc	tgcacagaag	180
cgcagaagca	aagcccaggc	agaaccatgc	taaccttaca	gctcagcctg	cacagaagcg	240
cagaagcaaa	gcccaggcag	aacatgctaa	ccttacagct	cagcctgcac	agaagcacag	300
a						301

<210> 283

<211> 301

<212> DNA

<213> Homo sapien

<400> 283

atctgtatcac	ggcagacaaa	ctttatarag	tgtagagagg	tgagcgaaag	gatgcaaaag	60
cactttgagg	gctttataat	aatatgctgc	ttgaaaaaaa	aaatgtgtag	ttgatactca	120
gtgcatctcc	agacatagta	aggggttgct	ctgaccaatc	aggatgatcat	tttttctatc	180
acttcccagg	ttttatgcaa	aaattttgtt	aaattctata	atgggtgatat	gcattctttta	240
ggaaacatat	acatttttta	aaatctattt	tatgtaagaa	ctgacagacg	aatttgcttt	300
g						301

<210> 284

<211> 301

<212> DNA

<213> Homo sapien

<400> 284

caggtacaaa	acgtatttaa	gtggccttaga	atttgaacat	ttgtgggtcct	tatttacttt	60
gcttcgtgtg	tgggcaaagc	aacatcttcc	ctaaatatat	attaccaaga	aaagcaagaa	120
gcagattagg	tttttgacaa	aacaaacagg	ccaaaggggg	gctgacctgg	agcagagcat	180
ggtgagaggc	aaggcatgag	agggcaagtt	tgttgtggac	agatctgtgc	ctactttatt	240
actggagtaa	aagaaaacaa	agttcattga	tgtcgaagga	tatatacagt	gttagaaatt	300
a						301

<210> 285

<211> 301

<212> DNA

<213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(301)
 <223> n = A,T,C or G

<400> 285
 acatcacccat gatcggatcc cccacccatt atacgttgta tgtttacata aatactcttc 60
 aatgatcatt agtggttttaa aaaaaatact gaaaactcct tctgcatccc aatctctaac 120
 caggaaagca aatgctatct acagacctgc aagccctccc tcaaacnaaa ctatttctgg 180
 attaaatatg tctgacttct tttgaggtca cactgactagg caaatgctat ttacgatctg 240
 caaaagctgt ttgaagagtc aaagccccca tgtgaacacg atttctggac cctgtaacag 300
 t 301

<210> 286
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 286
 taccactgca ttccagcctg ggtgacagag tgagactccg tctccaaaaa aaactttgct 60
 tgtatattat ttttgcctta cagtggatca ttctagtagg aaaggacagt aagatttttt 120
 atcaaaatgt gtcatgccag taagagatgt tatattcttt tctcatttct tccccacca 180
 aaaataagct accatatagc ttataagtct caaatTTTTTg ccttttacta aaatgtgatt 240
 gtttctgttc attgtgtatg cttcatcacc tatattaggc aaattccatt ttttcccttg 300
 t 301

<210> 287
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 287
 tacagatctg ggaactaaat attaaaaatg agtggtgctg gatatatgga gaatgttggg 60
 cccagaagga acgtagagat cagatattac aacagctttg ttttgagggg tagaaatatg 120
 aaatgatttg gttatgaacg cacagttagg gcagcagggc cagaatcctg accctctgcc 180
 ccgtgggtat ctctcctcca gcttggctgc ctcatgttat cacagtattc cattttgttt 240
 gttgcatgtc ttgtgaagcc atcaagattt tctcgtctgt tttcctctca ttggtaatgc 300
 t 301

<210> 288
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 288
 gtacaccta ctgcaaggac agctgaggaa tgtaatgggc agccgctttt aaagaagtag 60
 agtcaatagg aagacaaatt ccagttccag ctcagtctgg gtatctgcaa agctgcaaaa 120
 gatcttttaa gacaatttca agagaatatt tccttaaagt tggcaatttg gagatcatal 180
 aaaagcatct gcttttgtga tttaatttag ctcatctggc cactggaaga atccaaacag 240
 tctgccttaa ttttggatga atgcatgatg gaaattcaat aatttagaaa gttaaaaaaa 300
 a 301

<210> 289
 <211> 301

006280"062860

gtactctttc	tctccctcc	tctgaattta	attctttcaa	cttgcaattt	gcaaggatta	60
cacattttac	tgtgatgtat	attgtgttgc	aaaaaaaaa	gtgtctttgt	ttaaaattac	120
ttggtttg	aatccatctt	gctttttccc	cattggaact	agtcattaac	ccatctctga	180
actggtagaa	aaacrtctga	agagctagtc	tatcagcatc	tgacagggtga	attggatggg	240
tctcagaacc	atttcaccca	gacagcctgt	ttctatcctg	tttaataaat	tagtttgggt	300
tctct						305

<400> 299
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 tcaactgcacc ctctgcctcc cagggttcgag caattctcct gcctcagcct cccaggtagc 120
 tgggattgca ggctcacgcc accataccca gctaattttt ttgtattttt agtagagacg 180
 gagtttcgcc atgttggcca gctggtctca aactcctgac ctcaagcgac ctgcctgcct 240
 cggcctccca aagtgcctgga attataggca tgagtcaaca cgcccagcct aaagatatatt 300
 t 301

<210> 300
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 300
 attcagtttt atttgctgcc ccagtatctg taaccaggag tgccacaaaa tcttgccaga 60
 tatgtcccac acccactggg aaaggtctcc acctggctac ttctctatc agctgggtca 120
 gctgcattcc acaaggttct cagcctaata agtttacta cctgccagtc tcaaaactta 180
 gtaaagcaag accatgacat tccccacgg aaatcagagt ttgccccacc gtcttggttac 240
 tataaagcct gcctctaaca gtccttgctt cttcacacca atcccagcgc catcccccat 300
 g 301

<210> 301
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 301
 tttaaatttt gagaggataa aaaggacaaa taatctagaa atgtgtcttc ttcagtctgc 60
 agaggacccc aggtctccaa gcaaccacat ggtcaagggc atgaataatt aaaagttggt 120
 gggaactcac aaagaccctc agagctgaga caccacaac agtgggagct cacaagacc 180
 ctgagagctg agacaccac aacagtggga gctcacaag accctcagag ctgagacacc 240
 cacaacagca cctcgttcag ctgccacatg tgtgaataag gatgcaatgt ccagaagtgt 300
 t 301

<210> 302
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 302
 aggtacacat ttagcttggt gtaaagtact cacaaaactg attttaaaat caagttaatg 60
 tgaattttga aaattactac ttaatcctaa ttcacaataa caatggcatt aaggtttgac 120
 ttgagttggt tcttagtatt atttatggta aataggctct taccacttgc aaataactgg 180
 ccacatcatt aatgactgac ttcccagtaa ggctctctaa ggggtaagta ggaggatcca 240
 caggatttga gatgctaagg ccccagagat cgtttgatcc aaccctctta ttttcagagg 300
 g 301

<210> 303
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 303
 aggtaccaac tgtggaaata ggtagaggat cattttttct ttccatatca actaagttgt 60

```

atattgtttt ttgacagttt aacacatctt cttctgtcag agattctttc acaatagcac 120
tggctaattg aactaccgct tgcattgtta aaatgggtgt ttgtgaaatg atcataggcc 180
agtaacgggt atgtttttct aactgatctt ttgctcgttc caaagggacc tcaagacttc 240
catcgatttt atatctgggg tctagaaaag gagttaatct gttttccctc ataaattcac 300
c 301

```

```

<210> 304
<211> 301
<212> DNA
<213> Homo sapien

```

```

<400> 304
acatggatgt tattttgcag actgtcaacc tgaatttgta tttgcttgac attgcctaata 60
tattagtttc agtttcagct taccactttt ttgtctgcaa catgcaraas agacagtgcc 120
cttttttagtg tatcatatca ggaatcatct cacattgggt ttgtgccatta ctggtgcagt 180
gacttttcagc cacttgggta aggtggagtt ggccatatgt ctccactgca aaattactga 240
ttttcctttt gtaattaata agtgtgtgtg tgaagattct ttgagatgag gtatatatct 300
c 301

```

```

<210> 305
<211> 301
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

```

```

<400> 305
gangtacagc gtggtcaagg taacaagaag aaaaaaatgt gagtggcatc ctgggatgag 60
cagggggaca gacctggaca gacacgttgt catttgctgc tgtgggtagg aaaatgggag 120
taaaggagga gaaacagata caaaatctcc aactcagtat taaggatttc tcatgcctag 180
aatattggta gaaacaagaa tacattcata tggcaaataa ctaaccatgg tggaacaaaa 240
ttctgggatt taagtgggat accaangaaa ttgtattaaa agagctgttc atggaataag 300
a 301

```

```

<210> 306
<211> 8
<212> PRT
<213> Homo sapien

```

```

<400> 306
Val Leu Gly Trp Val Ala Glu Leu
1 5

```

```

<210> 307
<211> 637
<212> DNA
<213> Homo sapien

```

```

<400> 307
acaggggatg aagggaaagg gagaggatga ggaagcccc ctggggattt ggtttggtcc 60
ttgtgatcag gtggtctatg gggcttatcc ctacaaagaa gaatccagaa ataggggcac 120

```



```

attgaggaat gatacttgag cccaaagagc attcaatcat tgttttattt gccttmtttt 180
cacaccattg gtgagggagg gattaccacc ctgggggttat gaagatgggtt gaacacccca 240
cacatagcac cggagatatg agatcaacag tttcttagcc atagagattc acagcccaga 300
gcaggaggac gcttgcacac catgcaggat gacatggggg atgcgctcgg gattggtgtg 360
aagaagcaag gactgttaga ggcaggcttt atagtaacaa gacggtgggg caaactctga 420
tttccgtggg ggaatgtcat ggtcttgctt tactaagttt tgagactggc aggtagtga 480
actcattagg ctgagaacct tgtggaatgc acttgacca sctgatagag gaagtagcca 540
ggtgggagcc tttcccagtg ggtgtgggac atatctggca agattttgtg gcactcctgg 600
ttacagatac tggggcagca aataaaaactg aatcttg 637

```

<210> 308

<211> 647

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(647)

<223> n = A,T,C or G

<400> 308

```

acgattttca ttatcatgta aatcgggtca ctcaaggggc caaccacagc tgggagccac 60
tgctcagggg aaggttcata tgggactttc tactgccccaa ggttctatac aggatataaa 120
ggngcctcac agtatagatc tggtagcaaa gaagaagaaa caaactctga tctctttctg 180
ccacccctct gacccttttg aactcctctg accctttaga acaagcctac ctaatatctg 240
ctagagaaaa gaccaacaac ggcctcaaaag gatctcttac catgaaggtc tcagctaatt 300
cttggctaag atgtgggttc cacattagggt tctgaatatg gggggaaggg tcaatttgct 360
cattttgtgt gtggataaaag tcaggatgcc cagggggccag agcagggggc tgcttgcttt 420
gggaacaatg gctgagcata taaccatagg ttatggggaa caaaacaaca tcaaagtcac 480
tgtatcaatt gccatgaaga cttgagggag ctgaatctac cgattcatct taaggcagca 540
ggaccagttt gagtggcaac aatgcagcag cagaatcaat ggaaacaaca gaatgattgc 600
aatgtccttt tttttctcct gcttctgact tgataaaagg ggaccgt 647

```

<210> 309

<211> 460

<212> DNA

<213> Homo sapien

<400> 309

```

actttatagt ttaggctgga cattggaaaa aaaaaaagc cagaacaaca tgtgatagat 60
aatatgattg gctgcacact tccagactga tgaatgatga acgtgatgga ctattgtatg 120
gagcacatct tcagcaagag ggggaaatac tcatcatttt tggccagcag ttgtttgatc 180
accaaacatc atgccagaat actcagcaaa ccttcttagc tcttgagaag tcaaagtcag 240
ggggaattta ttcctggcaa ttttaattgg actccttatg tgagagcagc ggctaccag 300
ctgggggtggg ggagcgaacc cgtcactagt ggacatgcag tggcagagct cctggtaacc 360
acctagagga atacacaggc acatgtgtga tgccaagcgt gacacctgta gcactcaa 420
ttgtcttggt tttgtctttc ggtgtgtaag attcttaagt 460

```

<210> 310

<211> 539

<212> DNA

<213> Homo sapien

<400> 310

```

acgggactta tcaaataaag ataggaaaag aagaaaactc aaatattata ggcagaaatg      60
ctaaaggttt taaaatatgt caggattgga agaaggcatg gataaagaac aaagttcagt    120
taggaaaagag aaacacagaa ggaagagaca caataaaagt cattatgtat tctgtgagaa    180
gtcagacagt aagatttggt ggaaatgggt tggtttggtt tatggtatgt attttagcaa    240
taatctttat ggcagagaaa gctaaaatcc ttttagcttgc gtgaatgatc acttgctgaa    300
ttcctcaagg taggcatgat gaaggagggt ttagaggaga cacagacaca atgaactgac    360
ctagatagaa agccttagta tactcagcta ggaatagtga ttctgagggc aactgtgac     420
atgattatgt cattacatgt atggtagtga tggggatgat aggaaggaag aacttatggc    480
atattttcac cccacaaaaa gtcagttaaa tattgggaca ctaaccatcc aggtcaaga    539

```

```

<210> 311
<211> 526
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(526)
<223> n = A,T,C or G

```

```

<400> 311
caaatttgag ccaatgacat agaattttac aaatcaagaa gcttattctg gggccatttc      60
ttttgacgtt ttctctaaac tactaaagag gcattaatga tccataaatt atattatcta    120
catttacagc atttaaaatg tggttcagcat gaaatattag ctacagggga agctaaataa    180
attaaacatg gaataaagat ttgtccttaa atataatcta caagaagact ttgatatttg    240
tttttcacaa gtgaagcatt cttataaagt gtcataacct ttttggggaa actatgggaa    300
aaaatgggga aactctgaag ggttttaagt atcttacctg aagctacaga ctccataacc    360
tctctttaca gggagctcct gcagccccta cagaaatgag tggctgagat tcttgattgc    420
acagcaagag cttctcatct aaaccctttc cctttttagt atctgtgtat caagtataaa    480
agttctataa actgtagtnt acttatttta atccccaaag cacagt                    526

```

```

<210> 312
<211> 500
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(500)
<223> n = A,T,C or G

```

```

<400> 312
cctctctctc cccaccccct gactctagag aactggggtt tctcccagta ctccagcaat      60
tcattttctga aagcagttga gccactttat tccaaagtac actgcagatg ttcaaactct    120
ccattttctct ttcccttcca cctgccagtt ttgctgactc tcaacttgct atgagtgtaa    180
gcattaagga cattatgctt cttcgattct gaagacaggc cctgctcatg gatgactctg    240
gcttcttagg aaaatathtt tcttccaaaa tcagtaggaa atctaaactt atcccctctt    300
tgcagatgtc tagcagcttc agacatttgg ttaagaacct atgggaaaaa aaaaaatcct    360
tgctaattgt gtttcctttg taaaccanga ttcttatttg nctgggtatag aatatcagct    420
ctgaacgtgt ggtaaagatt tttgtgtttg aatataggag aaatcagttt gctgaaaagt    480
tagtcttaat tatctattgg

```

```

<210> 313
<211> 718

```

```
<220>  
<221> misc_feature  
<222> (1)...(718)  
<223> n = A,T,C or G
```

```
<210> 314
<211> 358
<212> DNA
<213> Homo sapien
```

```
<210> 315
<211> 341
<212> DNA
<213> Homo sapien
```

```
<210> 316
<211> 151
<212> DNA
<213> Homo sapien
```

<400> 316

```
<210> 317
<211> 151
<212> DNA
<213> Homo sapien
```

```
<210> 318
<211> 151
<212> DNA
<213> Homo sapien
```

```
<210> 319
<211> 151
<212> DNA
<213> Homo sapien
```

```
<210> 320
<211> 150
<212> DNA
<213> Homo sapien
```

```
<210> 321
<211> 151
<212> DNA
<213> Homo sapien
```

```

      <400> 321
agcaactttg tttttcatcc aggttatttt aggcttagga tttcctctca cactgcagtt      60
taggggtggca ttgtaaccag ctatggcata ggtgttaacc aaaggctgag taaacatggg    120
tgctctctgag aaatcaaaagt cttcatacac t                                     151

```

<210> 322
 <211> 151
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(151)
 <223> n = A,T,C or G

<400> 322
 atccagcatc ttctcctgtt tcttgccctc ctttttcttc ttcttasatt ctgcttgagg 60
 tttgggcttg gtcagtttgc cacagggctt ggagatgggt acagtcttct ggcattcggc 120
 attgtgcagg gctcgcttca nacttccagt t 151

<210> 323
 <211> 151
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(151)
 <223> n = A,T,C or G

<400> 323
 tgaggacttg tktttctttt ctttattttt aatcctctta ckttgtaa atattgccta 60
 nagactcant tactaccag tttgtgggtt twtgggagaa atgtaactgg acagttagct 120
 gttcaatyaa aaagacactt ancccatgtg g 151

<210> 324
 <211> 461
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(461)
 <223> n = A,T,C or G

<400> 324
 acctgtgtgg aatttcagct ttctcatgc aaaaggattt tgtatccccg gcttacttga 60
 agaagtgggc agctaaagga atccagggtt ttggttggtg tgtaataacc tttgatgaaa 120
 agagttacta cgaatcccat cttgggtcca gctatatcac tgacagcatg gtagaagact 180
 gcgaacctca cttctagact ttcaagggtg gacgaaacgg gttcagaaac tgccaggggc 240
 ctcatacagg gatatacaaa taccctttgt gctaccagg ccctggggaa tcaggtgact 300
 cacacaaatg caatagttgg tcaactgcatt tttacctgaa ccaaagctaa acccggtgtt 360
 gccaccatgc accatggcat gccagagttc aacactgttg ctcttgaaaa ttgggtctga 420
 aaaaacgcac aagagcccct gccctgccct agctgangca c 461

<210> 325
 <211> 400
 <212> DNA
 <213> Homo sapien

<400> 325

acactgtttc	catgttatgt	ttctacacat	tgctacctca	gtgctcctgg	aaacttagct	60
tttgatgtct	ccaagtagtc	caccttcatt	taactctttg	aaactgtatc	atctttgccca	120
agtaagagtg	gtggcctatt	tcagctgctt	tgacaaaatg	actggctcct	gacttaacgt	180
tctataaatg	aatgtgctga	agcaaagtgc	ccatgggtggc	ggcgaagaag	agaaagatgt	240
gttttgtttt	ggactctctg	tggtcccttc	caatgctgtg	ggtttccaac	caggggaagg	300
gtcccttttg	cattgccaaag	tgccataacc	atgagcacta	cgctaccatg	gttctgcctc	360
ctggccaagc	aggtcggttt	gcaagaatga	aatgaatgat			400

<210> 326

<211> 1215

<212> DNA

<213> Homo sapien

<400> 326

ggaggactgc	agcccgcaact	cgcagccctg	gcaggcggca	ctgggtcatgg	aaaacgaatt	60
gttctgctcg	ggcgctcctgg	tgcatecgca	gtgggtgctg	tcagccgcac	actgtttcca	120
gaactcctac	accatcgggc	tgggcctgca	cagtcttgag	gccgaccaag	agccagggag	180
ccagatggtg	gaggccagcc	tctccgtacg	gcacccagag	tacaacagac	ccttgctcgc	240
taacgacctc	atgctcatca	agttggacga	atccgtgtcc	gagtctgaca	ccatccggag	300
catcagcatt	gcttcgcagt	gccctaccgc	ggggaaactct	tgctcgtttt	ctggctgggg	360
tctgctggcg	aacggcagaa	tgctaccgt	gctgcagtgc	gtgaacgtgt	cggtggtgtc	420
tgaggagggtc	tgcaagtaagc	tctatgaccc	gctgtaccac	cccagcatgt	tctgcgcggg	480
cggagggcaa	gaccagaagg	actcctgcaa	cgggtgactct	ggggggcccc	tgatctgcaa	540
cgggtacttg	cagggccttg	tgtctttcgg	aaaagccccg	tgtggccaag	ttggcgtgcc	600
aggtgtctac	accaacctct	gcaaattcac	tgagtggata	gagaaaaccg	tccaggccag	660
ttaactcttg	ggactgggaa	cccatgaaat	tgacccccaa	atacatcctg	cggaaggaaat	720
tcaggaatat	ctgttcccag	ccctcctcc	ctcaggccca	ggagtccagg	ccccagccc	780
ctcctccctc	aaaccaaggg	tacagatccc	cagccctccc	tcctcagac	ccaggagtcc	840
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ggagtccaga	ccccccagcc	cctcctccct	cagacccagg	ggtccaggcc	cccaaccctt	960
cctccctcag	actcagaggt	ccaagcccc	aacccctcct	tccccagacc	cagaggtcca	1020
ggtcccagcc	cctcctccct	cagacccagc	ggtccaatgc	cacctagact	ctccctgtac	1080
acagtgcccc	cttgtggcac	gttgacccaa	ccttaccagt	tggtttttca	ttttttgtcc	1140
ctttccctta	gatccagaaa	taaagtctaa	gagaagcgca	aaaaaaaaaa	aaaaaaaaaa	1200
aaaaaaaaaa	aaaaa					1215

<210> 327

<211> 220

<212> PRT

<213> Homo sapien

<400> 327

Glu Asp Cys Ser Pro His Ser Gln Pro Trp Gln Ala Ala Leu Val Met	
1 5 10 15	
Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln Trp Val	
20 25 30	
Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu Gly	
35 40 45	
Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val Glu	
50 55 60	
Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu Leu Ala	
65 70 75 80	

Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser Asp
 85 90 95
 Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly Asn
 100 105 110
 Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg Met Pro
 115 120 125
 Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu Glu Val Cys
 130 135 140
 Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys Ala Gly
 145 150 155 160
 Gly Gly Gln Asp Gln Lys Asp Ser Cys Asn Gly Asp Ser Gly Gly Pro
 165 170 175
 Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly Lys Ala
 180 185 190
 Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn Leu Cys Lys
 195 200 205
 Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser
 210 215 220

<210> 328
 <211> 234
 <212> DNA
 <213> Homo sapien

<400> 328
 cgctcgtctc tggtagctgc agccaaatca taaacggcga ggactgcagc ccgcactcgc 60
 agccctggca ggcggcactg gtcattgaaa acgaattgtt ctgctcgggc gtcctgggtgc 120
 atccgcagtg ggtgctgtca gccacacact gtttccagaa ctctacacc atcgggctgg 180
 gctgcacag tcttgaggcc gaccaagagc cagggagcca gatggtggag gcca 234

<210> 329
 <211> 77
 <212> PRT
 <213> Homo sapien

<400> 329
 Leu Val Ser Gly Ser Cys Ser Gln Ile Ile Asn Gly Glu Asp Cys Ser
 1 5 10 15
 Pro His Ser Gln Pro Trp Gln Ala Ala Leu Val Met Glu Asn Glu Leu
 20 25 30
 Phe Cys Ser Gly Val Leu Val His Pro Gln Trp Val Leu Ser Ala Thr
 35 40 45
 His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu Gly Leu His Ser Leu
 50 55 60
 Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val Glu Ala
 65 70 75

<210> 330
 <211> 70
 <212> DNA
 <213> Homo sapien

<400> 330
 cccaacacaa tggcccgatc ccattcctga ctccgccctc aggatcgctc gtctctggta 60

gctgcagcca

70

<210> 331
 <211> 22
 <212> PRT
 <213> Homo sapien

<400> 331
 Gln His Asn Gly Pro Ile Pro Ser Leu Thr Pro Pro Ser Gly Ser Leu
 1 5 10 15
 Val Ser Gly Ser Cys Ser
 20

<210> 332
 <211> 2507
 <212> DNA
 <213> Homo sapien

<400> 332
 tgggtgccgct gcagccggca gagatgggtg agctcatggt cccgctggtg ctccctcttc 60
 tgcccttcct tctgtatatg gctgcgcccc aaatcaggaa aatgctgtcc agtgggggtgt 120
 gtacatcaac tggttcagctt cctgggaaag tagttgtggt cacaggagct aatacaggta 180
 tcgggaagga gacagccaaa gagctggctc agagaggagc tcgagtatat ttagcttgcc 240
 gggatgtgga aaagggggaa ttgggtggcca aagagatcca gaccacgaca ggggaaccagc 300
 aggtgttggt gcggaaaactg gacctgtctg atactaagtc tattcgagct tttgctaagg 360
 gttcttagc tgaggaaaag cacctccacg ttttgatcaa caatgcagga gtgatgatgt 420
 gtccgtactc gaagacagca gatggctttg agatgcacat aggagtcaac cacttgggtc 480
 acttcctcct aaccatctg ctgctagaga aactaaagga atcagcccca tcaaggatag 540
 taaatgtgtc ttccctcgca catcacctgg gaaggatcca cttccataac ctgcagggcg 600
 agaaattcta caatgcaggc ctggcctact gtcacagcaa gctagccaac atcctcttca 660
 cccaggaact ggcccggaaga ctaaaaggct ctggcggttac gacgtattct gtacaccctg 720
 gcacagtcca atctgaactg gttcggcact catctttcat gagatggatg tgggtggcttt 780
 tctccttttt catcaagact cctcagcagg gagcccagac cagcctgcac tgtgccttaa 840
 cagaaggtct tgagattcta agtgggaatc atttcagtga ctgtcatgtg gcatgggtct 900
 ctgcccgaagc tcgtaatgag actatagcaa ggcggctgtg ggacgtcagt tgtgacctgc 960
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 agagagcaaaa acctccagc cttgcctgct tgggtgtccag ttaaaaactca gtgtactgcc 1140
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 cttagagatat cataatagga taagaagacc ctcatatgac ctgcacagct cattttcctt 1260
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<211> 3030

<212> DNA

<213> Homo sapien

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<212> DNA

<213> Homo sapien

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<212> DNA
<213> Homo sapien
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<210> 339
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 <212> PRT
 <213> Homo sapien

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 Cys Thr Ser Thr Val Gln Leu Pro Gly Lys Val Val Val Thr Gly
 35 40 45
 Ala Asn Thr Gly Ile Gly Lys Glu Thr Ala Lys Glu Leu Ala Gln Arg
 50 55 60
 Gly Ala Arg Val Tyr Leu Ala Cys Arg Asp Val Glu Lys Gly Glu Leu
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 Val Ala Lys Glu Ile Gln Thr Thr Thr Gly Asn Gln Gln Val Leu Val
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 Arg Lys Leu Asp Leu Ser Asp Thr Lys Ser Ile Arg Ala Phe Ala Lys
 100 105 110
 Gly Phe Leu Ala Glu Glu Lys His Leu His Val Leu Ile Asn Asn Ala
 115 120 125
 Gly Val Met Met Cys Pro Tyr Ser Lys Thr Ala Asp Gly Phe Glu Met
 130 135 140
 His Ile Gly Val Asn His Leu Gly His Phe Leu Leu Thr His Leu Leu
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 Ser Leu Ala His His Leu Gly Arg Ile His Phe His Asn Leu Gln Gly
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 Glu Lys Phe Tyr Asn Ala Gly Leu Ala Tyr Cys His Ser Lys Leu Ala
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<400> 340

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<210> 341

<211> 344

<212> DNA

<213> Homo sapien

<400> 341

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<211> 592

<212> DNA

<213> Homo sapien

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<211> 382

<212> DNA

<213> Homo sapien

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<210> 348
<211> 251
<212> DNA
<213> Homo sapien

<400> 348
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<210> 349
<211> 251
<212> DNA
<213> Homo sapien

<400> 349
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<210> 350
<211> 908
<212> DNA
<213> Homo sapien

<400> 350
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<400> 351

<400> 352

<400> 353

<400> 354

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<210> 355

<211> 676

<212> DNA

<213> Homo sapien

<400> 355

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<210> 356

<211> 574

<212> DNA

<213> Homo sapien

<400> 356

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gagttctttt	cttgggcaac	agataaccag	acaggactct	aatcgtgtct	ttattcaaca	360
ttcttctgtc	tctgcctaga	ctggaataaa	aagccaatct	ctctcgtggc	acagggaagg	420
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<210> 357

<211> 393

<212> DNA

<213> Homo sapien

<400> 357

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gcataatctg	tacaaaatta	aactgtcctt	tttggcattt	taacaaattt	gcaacgktct	360
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<210> 358
 <211> 630
 <212> DNA
 <213> Homo sapien

<400> 358						
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<210> 359
 <211> 620
 <212> DNA
 <213> Homo sapien

<400> 359						
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 <213> Homo sapien

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<210> 361
<211> 351
<212> DNA
<213> Homo sapien

<400> 361
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<210> 362
<211> 463
<212> DNA
<213> Homo sapien

<400> 362
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<210> 363
<211> 653
<212> DNA
<213> Homo sapien

<220>
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<210> 365
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 <212> DNA
 <213> Homo sapien

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<210> 366
 <211> 1851
 <212> DNA
 <213> Homo sapien

<400> 366
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<210> 367

<211> 668

<212> DNA

<213> Homo sapien

<400> 367

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<210> 368

<211> 1512

<212> DNA

<213> Homo sapien

<400> 368

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<210> 369

<211> 1853

<212> DNA

<213> Homo sapien

<400> 369

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<210> 370

<211> 2184

<212> DNA

<213> Homo sapien

<400> 370

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<210> 372

<211> 1059

<212> DNA

<213> Homo sapien

<400> 372

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<210> 373

<211> 1155

<212> DNA

<213> Homo sapien

<400> 373

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<210> 374

<211> 2000

<212> DNA

<213> Homo sapien

<400> 374

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<210> 375

<211> 2040

<212> DNA

<213> Homo sapien

<400> 375

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<210> 376

<211> 329

<212> PRT

<213> Homo sapien

<400> 376

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      35          40          45
Leu Asp Gly Gln Gly Glu Arg Gln Glu Gln Arg Gly His Phe Trp Arg
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Pro Gln Arg Leu Leu Cys Glu Asp Ala Trp Glu Gln Glu Val Gln Val
      65          70          75          80
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Val Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe Met Asp Pro Arg Tyr
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His Val His Gly Glu Asp Leu Asp Lys Leu His Arg Ala Ala Trp Trp
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Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met Leu Arg Asp Thr Asp
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Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr Ala Leu Thr Lys Ala
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Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met Leu Leu Glu His Gly
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Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr
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Ala Val Tyr Asn Glu Asp Lys Leu Met Ala Lys Ala Leu Leu Leu Tyr
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      260          265          270
Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr Gly Arg Thr Ala Leu
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Ile Leu Ala Val Cys Cys Gly Ser Ala Ser Ile Val Ser Pro Leu Leu
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<210> 377

<211> 148

<212> PRT

<213> Homo sapien

<220>

<221> VARIANT

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<222> (1)...(148)

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<400> 377

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Val Val Lys Leu Xaa Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp
65          70          75          80
Asn Lys Lys Arg Thr Ala Leu Xaa Lys Ala Val Gln Cys Gln Glu Asp
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Glu Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro
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Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr Ala Xaa Tyr Asn Glu Asp
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<210> 378

<211> 1719

<212> PRT

<213> Homo sapien

<400> 378

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Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val
65          70          75          80
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Arg Ala Ala Trp Trp Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met
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Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu Val Val Lys Leu Leu

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Leu	Thr	Pro	Leu	Leu	Leu	Gly	Val	His	Glu	Gln	Lys	Gln	Gln	Val	Val										
				275							280														
Lys	Phe	Leu	Ile	Lys	Lys	Lys	Ala	Asn	Leu	Asn	Ala	Leu	Asp	Arg	Tyr										
	290					295					300														
Gly	Arg	Thr	Ala	Leu	Ile	Leu	Ala	Val	Cys	Cys	Gly	Ser	Ala	Ser	Ile										
305					310						315														
Val	Ser	Leu	Leu	Leu	Glu	Gln	Asn	Ile	Asp	Val	Ser	Ser	Gln	Asp	Leu										
				325							330														
Ser	Gly	Gln	Thr	Ala	Arg	Glu	Tyr	Ala	Val	Ser	Ser	His	His	His	Val										
				340							345														
Ile	Cys	Gln	Leu	Leu	Ser	Asp	Tyr	Lys	Glu	Lys	Gln	Met	Leu	Lys	Ile										
				355							360														
Ser	Ser	Glu	Asn	Ser	Asn	Pro	Glu	Asn	Val	Ser	Arg	Thr	Arg	Asn	Lys										
				370							380														
Pro	Arg	Thr	His	Met	Val	Val	Glu	Val	Asp	Ser	Met	Pro	Ala	Ala	Ser										
385					390						395														
Ser	Val	Lys	Lys	Pro	Phe	Gly	Leu	Arg	Ser	Lys	Met	Gly	Lys	Trp	Cys										
				405							410														
Cys	Arg	Cys	Phe	Pro	Cys	Cys	Arg	Glu	Ser	Gly	Lys	Ser	Asn	Val	Gly										
				420							425														
Thr	Ser	Gly	Asp	His	Asp	Asp	Ser																		

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Glu Tyr Gly Asn Thr	Thr Leu His Tyr Ala Ile Tyr Asn Glu Asp Lys				
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Leu Met Ala Lys Ala	Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser Lys				
	645		650		655
Asn Lys His Gly Leu Thr	Pro Leu Leu Leu Gly Val His Glu Gln Lys				
	660		665		670
Gln Gln Val Val Lys Phe	Leu Ile Lys Lys Lys Ala Asn Leu Asn Ala				
	675		680		685
Leu Asp Arg Tyr Gly Arg	Thr Ala Leu Ile Leu Ala Val Cys Cys Gly				
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Ser Ala Ser Ile Val	Ser Leu Leu Leu Glu Gln Asn Ile Asp Val Ser				
705		710		715	720
Ser Gln Asp Leu Ser	Gly Gln Thr Ala Arg Glu Tyr Ala Val Ser Ser				
	725		730		735
His His His Val Ile	Cys Gln Leu Leu Ser Asp Tyr Lys Glu Lys Gln				
	740		745		750
Met Leu Lys Ile Ser	Ser Glu Asn Ser Asn Pro Glu Gln Asp Leu Lys				
	755		760		765
Leu Thr Ser Glu Glu	Glu Ser Gln Arg Phe Lys Gly Ser Glu Asn Ser				
	770		775		780
Gln Pro Glu Lys Met	Ser Gln Glu Pro Glu Ile Asn Lys Asp Gly Asp				
785		790		795	800
Arg Glu Val Glu Glu	Glu Met Lys Lys His Glu Ser Asn Asn Val Gly				
	805		810		815
Leu Leu Glu Asn Leu	Thr Asn Gly Val Thr Ala Gly Asn Gly Asp Asn				
	820		825		830
Gly Leu Ile Pro Gln	Arg Lys Ser Arg Thr Pro Glu Asn Gln Gln Phe				
	835		840		845
Pro Asp Asn Glu Ser	Glu Glu Tyr His Arg Ile Cys Glu Leu Val Ser				
	850		855		860
Asp Tyr Lys Glu Lys	Gln Met Pro Lys Tyr Ser Ser Glu Asn Ser Asn				
865		870		875	880
Pro Glu Gln Asp Leu	Lys Leu Thr Ser Glu Glu Glu Ser Gln Arg Leu				
	885		890		895
Glu Gly Ser Glu Asn	Gly Gln Pro Glu Leu Glu Asn Phe Met Ala Ile				
	900		905		910
Glu Glu Met Lys Lys	His Gly Ser Thr His Val Gly Phe Pro Glu Asn				
	915		920		925
Leu Thr Asn Gly Ala	Thr Ala Gly Asn Gly Asp Asp Gly Leu Ile Pro				
	930		935		940
Pro Arg Lys Ser Arg	Thr Pro Glu Ser Gln Gln Phe Pro Asp Thr Glu				
945		950		955	960
Asn Glu Glu Tyr His	Ser Asp Glu Gln Asn Asp Thr Gln Lys Gln Phe				
	965		970		975
Cys Glu Glu Gln Asn	Thr Gly Ile Leu His Asp Glu Ile Leu Ile His				
	980		985		990
Glu Glu Lys Gln Ile	Glu Val Val Glu Lys Met Asn Ser Glu Leu Ser				
	995		1000		1005
Leu Ser Cys Lys Lys	Glu Lys Asp Ile Leu His Glu Asn Ser Thr Leu				
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Arg Glu Glu Ile Ala	Met Leu Arg Leu Glu Leu Asp Thr Met Lys His				
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Gln Ser Gln Leu Pro	Arg Thr His Met Val Val Glu Val Asp Ser Met				

006230" 334590

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 Pro Ala Ala Ser Ser Val Lys Lys Pro Phe Gly Leu Arg Ser Lys Met
 1060 1065 1070
 Gly Lys Trp Cys Cys Arg Cys Phe Pro Cys Cys Arg Glu Ser Gly Lys
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 Leu Arg Ser Lys Met Gly Lys Trp Cys Arg His Cys Phe Pro Cys Cys
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 Arg Gly Ser Gly Lys Ser Asn Val Gly Ala Ser Gly Asp His Asp Asp
 1125 1130 1135
 Ser Ala Met Lys Thr Leu Arg Asn Lys Met Gly Lys Trp Cys Cys His
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 Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Lys Val Gly Ala Trp
 1155 1160 1165
 Gly Asp Tyr Asp Asp Ser Ala Phe Met Glu Pro Arg Tyr His Val Arg
 1170 1175 1180
 Gly Glu Asp Leu Asp Lys Leu His Arg Ala Ala Trp Trp Gly Lys Val
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 Pro Arg Lys Asp Leu Ile Val Met Leu Arg Asp Thr Asp Val Asn Lys
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 Lys Asp Lys Gln Lys Arg Thr Ala Leu His Leu Ala Ser Ala Asn Gly
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 Asn Ser Glu Val Val Lys Leu Leu Asp Arg Arg Cys Gln Leu Asn
 1235 1240 1245
 Val Leu Asp Asn Lys Lys Arg Thr Ala Leu Ile Lys Ala Val Gln Cys
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 Gln Glu Asp Glu Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro
 1265 1270 1275 1280
 Asn Ile Pro Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr Ala Ile Tyr
 1285 1290 1295
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 Ile Glu Ser Lys Asn Lys His Gly Leu Thr Pro Leu Leu Leu Gly Val
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 His Glu Gln Lys Gln Gln Val Val Lys Phe Leu Ile Lys Lys Lys Ala
 1330 1335 1340
 Asn Leu Asn Ala Leu Asp Arg Tyr Gly Arg Thr Ala Leu Ile Leu Ala
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 Val Cys Cys Gly Ser Ala Ser Ile Val Ser Leu Leu Leu Glu Gln Asn
 1365 1370 1375
 Ile Asp Val Ser Ser Gln Asp Leu Ser Gly Gln Thr Ala Arg Glu Tyr
 1380 1385 1390
 Ala Val Ser Ser His His His Val Ile Cys Gln Leu Leu Ser Asp Tyr
 1395 1400 1405
 Lys Glu Lys Gln Met Leu Lys Ile Ser Ser Glu Asn Ser Asn Pro Glu
 1410 1415 1420
 Gln Asp Leu Lys Leu Thr Ser Glu Glu Glu Ser Gln Arg Phe Lys Gly
 1425 1430 1435 1440
 Ser Glu Asn Ser Gln Pro Glu Lys Met Ser Gln Glu Pro Glu Ile Asn
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<210> 379
<211> 656
<212> PRT
<213> Homo sapien
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<400> 379															
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			20					25					30		
Pro	Cys	Cys	Arg	Glu	Ser	Gly	Lys	Ser	Asn	Val	Gly	Thr	Ser	Gly	Asp
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His	Asp	Asp	Ser	Ala	Met	Lys	Thr	Leu	Arg	Ser	Lys	Met	Gly	Lys	Trp
	50					55					60				
Cys	Arg	His	Cys	Phe	Pro	Cys	Cys	Arg	Gly	Ser	Gly	Lys	Ser	Asn	Val
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Gly	Ala	Ser	Gly	Asp	His	Asp	Asp	Ser	Ala	Met	Lys	Thr	Leu	Arg	Asn
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Lys	Met	Gly	Lys	Trp	Cys	Cys	His	Cys	Phe	Pro	Cys	Cys	Arg	Gly	Ser
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Gly	Lys	Ser	Lys	Val	Gly	Ala	Trp	Gly	Asp	Tyr	Asp	Asp	Ser	Ala	Phe
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Leu	Asp	Arg	Arg	Cys	Gln	Leu	Asn	Val	Leu	Asp	Asn	Lys	Lys	Arg	Thr
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Ala	Leu	Ile	Lys	Ala	Val	Gln	Cys	Gln	Glu	Asp	Glu	Cys	Ala	Leu	Met
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Leu	Leu	Glu	His	Gly	Thr	Asp	Pro	Asn	Ile	Pro	Asp	Glu	Tyr	Gly	Asn
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Thr	Thr	Leu	His	Tyr	Ala	Ile	Tyr	Asn	Glu	Asp	Lys	Leu	Met	Ala	Lys
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Lys	Phe	Leu	Ile	Lys	Lys	Lys	Ala	Asn	Leu	Asn	Ala	Leu	Asp	Arg	Tyr
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Gly	Arg	Thr	Ala	Leu	Ile	Leu	Ala	Val	Cys	Cys	Gly	Ser	Ala	Ser	Ile
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Val	Ser	Leu	Leu	Leu	Glu	Gln	Asn	Ile	Asp	Val	Ser	Ser	Gln	Asp	Leu
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Ser	Gly	Gln	Thr	Ala	Arg	Glu	Tyr	Ala	Val	Ser	Ser	His	His	His	Val
			340				345						350		
Ile	Cys	Gln	Leu	Leu	Ser	Asp	Tyr	Lys	Glu	Lys	Gln	Met	Leu	Lys	Ile
		355				360						365			
Ser	Ser	Glu	Asn	Ser	Asn	Pro	Glu	Gln	Asp	Leu	Lys	Leu	Thr	Ser	Glu
	370					375					380				
Glu	Glu	Ser	Gln	Arg	Phe	Lys	Gly	Ser	Glu	Asn	Ser	Gln	Pro	Glu	Lys
385					390					395					400
Met	Ser	Gln	Glu	Pro	Glu	Ile	Asn	Lys	Asp	Gly	Asp	Arg	Glu	Val	Glu
				405					410					415	
Glu	Glu	Met	Lys	Lys	His	Glu	Ser	Asn	Asn	Val	Gly	Leu	Leu	Glu	Asn
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Leu	Thr	Asn	Gly	Val	Thr	Ala	Gly	Asn	Gly	Asp	Asn	Gly	Leu	Ile	Pro
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Gln	Arg	Lys	Ser	Arg	Thr	Pro	Glu	Asn	Gln	Gln	Phe	Pro	Asp	Asn	Glu
	450					455					460				
Ser	Glu	Glu	Tyr	His	Arg	Ile	Cys	Glu	Leu	Val	Ser	Asp	Tyr	Lys	Glu
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<210> 380
<211> 671
<212> PRT
<213> Homo sapien
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	<400>			380											
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			20					25					30		
Pro	Cys	Cys	Arg	Glu	Ser	Gly	Lys	Ser	Asn	Val	Gly	Thr	Ser	Gly	Asp
		35					40					45			
His	Asp	Asp	Ser	Ala	Met	Lys	Thr	Leu	Arg	Ser	Lys	Met	Gly	Lys	Trp
	50					55					60				
Cys	Arg	His	Cys	Phe	Pro	Cys	Cys	Arg	Gly	Ser	Gly	Lys	Ser	Asn	Val
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Gly	Ala	Ser	Gly	Asp	His	Asp	Asp	Ser	Ala	Met	Lys	Thr	Leu	Arg	Asn
				85					90					95	
Lys	Met	Gly	Lys	Trp	Cys	Cys	His	Cys	Phe	Pro	Cys	Cys	Arg	Gly	Ser
			100					105					110		
Gly	Lys	Ser	Lys	Val	Gly	Ala	Trp	Gly	Asp	Tyr	Asp	Asp	Ser	Ala	Phe
		115					120					125			
Met	Glu	Pro	Arg	Tyr	His	Val	Arg	Gly	Glu	Asp	Leu	Asp	Lys	Leu	His
	130					135					140				
Arg	Ala	Ala	Trp	Trp	Gly	Lys	Val	Pro	Arg	Lys	Asp	Leu	Ile	Val	Met
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Leu	Arg	Asp	Thr	Asp	Val	Asn	Lys	Lys	Asp	Lys	Gln	Lys	Arg	Thr	Ala
				165					170					175	
Leu	His	Leu	Ala	Ser	Ala	Asn	Gly	Asn	Ser	Glu	Val	Val	Lys	Leu	Leu
			180					185					190		
Leu	Asp	Arg	Arg	Cys	Gln	Leu	Asn	Val	Leu	Asp	Asn	Lys	Lys	Arg	Thr
		195					200					205			
Ala	Leu	Ile	Lys	Ala	Val	Gln	Cys	Gln	Glu	Asp	Glu	Cys	Ala	Leu	Met
	210					215					220				
Leu	Leu	Glu	His	Gly	Thr	Asp	Pro	Asn	Ile	Pro	Asp	Glu	Tyr	Gly	Asn
225					230					235					240
Thr	Thr	Leu	His	Tyr	Ala	Ile	Tyr	Asn	Glu	Asp	Lys	Leu	Met	Ala	Lys
				245					250					255	
Ala	Leu	Leu	Leu	Tyr	Gly	Ala	Asp	Ile	Glu	Ser	Lys	Asn	Lys	His	Gly
			260					265					270		
Leu	Thr	Pro	Leu	Leu	Leu	Gly	Val	His	Glu	Gln	Lys	Gln	Gln	Val	Val

275 280 285
 Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr
 290 295 300
 Gly Arg Thr Ala Leu Ile Leu Ala Val Cys Cys Gly Ser Ala Ser Ile
 305 310 315 320
 Val Ser Leu Leu Leu Glu Gln Asn Ile Asp Val Ser Ser Gln Asp Leu
 325 330 335
 Ser Gly Gln Thr Ala Arg Glu Tyr Ala Val Ser Ser His His Val
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 Ile Cys Gln Leu Leu Ser Asp Tyr Lys Glu Lys Gln Met Leu Lys Ile
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 Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp Leu Lys Leu Thr Ser Glu
 370 375 380
 Glu Glu Ser Gln Arg Phe Lys Gly Ser Glu Asn Ser Gln Pro Glu Lys
 385 390 395 400
 Met Ser Gln Glu Pro Glu Ile Asn Lys Asp Gly Asp Arg Glu Val Glu
 405 410 415
 Glu Glu Met Lys Lys His Glu Ser Asn Asn Val Gly Leu Leu Glu Asn
 420 425 430
 Leu Thr Asn Gly Val Thr Ala Gly Asn Gly Asp Asn Gly Leu Ile Pro
 435 440 445
 Gln Arg Lys Ser Arg Thr Pro Glu Asn Gln Gln Phe Pro Asp Asn Glu
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 Ser Glu Glu Tyr His Arg Ile Cys Glu Leu Val Ser Asp Tyr Lys Glu
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 Lys Gln Met Pro Lys Tyr Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp
 485 490 495
 Leu Lys Leu Thr Ser Glu Glu Glu Ser Gln Arg Leu Glu Gly Ser Glu
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 515 520 525
 Gly Asp Arg Glu Leu Glu Asn Phe Met Ala Ile Glu Glu Met Lys Lys
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 580 585 590
 Ser Asp Glu Gln Asn Asp Thr Gln Lys Gln Phe Cys Glu Glu Gln Asn
 595 600 605
 Thr Gly Ile Leu His Asp Glu Ile Leu Ile His Glu Glu Lys Gln Ile
 610 615 620
 Glu Val Val Glu Lys Met Asn Ser Glu Leu Ser Leu Ser Cys Lys Lys
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<210> 381

<211> 251

<212> DNA

<213> Homo sapien

<400> 381

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ccaatatccc	aggagaagca	ttggggaggt	gggggcaggt	gaaggacca	ggactcacac	180
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<210> 382

<211> 3279

<212> DNA

<213> Homo sapiens

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<210> 383

<211> 154

<212> PRT

<213> Homo sapiens

<400> 383

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His Cys Phe Ser Ser Glu Glu Ser Gly Ala Val Asp Gly Ala Gly Gln
      35                                40                                45

Lys Lys Asp Arg Ala Trp Leu Arg Cys Pro Glu Ala Val Ala Gly Phe
      50                                55                                60

Pro Leu Gly Ser Asp Cys Arg Glu Gly Gly Arg Gln Gly Cys Gly Gly
      65                                70                                75                                80

Ser Asp Asp Glu Asp Asp Leu Gly Val Ala Pro Gly Leu Ala Pro Ala
      85                                90                                95

Trp Ala Leu Thr Gln Pro Pro Ser Gln Ser Pro Gly Pro Gln Ser Leu
      100                               105                               110

Pro Ser Thr Pro Ser Ser Ile Trp Pro Gln Trp Val Ile Leu Ile Thr
      115                               120                               125

Glu Leu Thr Ile Pro Ser Pro Ala His Gly Pro Pro Trp Leu Pro Asn
      130                               135                               140

Ala Leu Glu Arg Gly His Leu Val Arg Glu
      145                               150

```

<210> 384

006230" 9625960

<211> 557
 <212> DNA
 <213> Homo sapiens

<400> 384
 ggatcctcta gagcggccgc ctactactac taaattcgcg gccgcgtcga cgaagaagag 60
 aaagatgtgt tttgttttgg actctctgtg gtcccttcca atgctgtggg tttccaacca 120
 ggggaagggt cccttttgca ttgccaagtg ccataaccat gagcactact ctaccatggg 180
 tctgcctcct ggccaagcag gctggtttgc aagaatgaaa tgaatgattc tacagctagg 240
 acttaacctt gaaatggaaa gtcttgcaat ccattttgca ggatccgtct gtgcacatgc 300
 ctctgtagag agcagcattc ccagggacct tggaaacagt tggcactgta aggtgcttgc 360
 tccccaaagac acatcctaata aggtgttgta atgggtgaaaa cgtcttcctt ctttattgcc 420
 ccttcttatt tatgtgaaca actgtttgtc tttttttgta tcttttttaa actgtaaagt 480
 tcaattgtga aaatgaatat catgcaaata aattatgcga tttttttttc aaagtaaaaa 540
 aaaaaaaaaa aaaaaaaa 557

<210> 385
 <211> 337
 <212> DNA
 <213> Homo sapiens

<400> 385
 ttcccagggt atgtgcgagg gaagacacat ttactatcct tgatggggct gattccttta 60
 gtttctctag cagcagatgg gttaggagga agtgacccaa gtggttgact cctatgtgca 120
 tctcaaagcc atctgctgtc ttogagtagc gacacatcat cactcctgca ttgttgatca 180
 aaacgtggag gtgcttttcc tcagctaaga agcccttagc aaaagctcga atagacttag 240
 tatcagacag gtccagtttc cgcaccaaca cctgctgggt cctgtcgtg gtctggatct 300
 ctttggccac caattcccc ttttccacat cccggca 337

<210> 386
 <211> 300
 <212> DNA
 <213> Homo sapiens

<400> 386
 gggcccgccta ccggcccagg cccgcctcgc cgagtcctcc tccccgggtg cctgcccgcga 60
 gcccgctcgcg ccagaggggt gggcgcgggg ctgcctctac cggctggcgg ctgtaactca 120
 gcgaccttgg cccgaaggct ctagcaaggga cccaccgacc ccagccgcgg cggcgggcgc 180
 gcggactttg cccggtgtgt ggggcgggagc ggactgcgtg tccgcggacg ggcagcgaag 240
 atgttagcct tcgctgccag gaccgtggac cgatcccagg gctgtggtgt aacctcagcc 300

<210> 387
 <211> 537
 <212> DNA
 <213> Homo sapiens

<400> 387
 gggccgagtc gggcaccaag ggactctttg caggcttcct tcctcggatc atcaaggctg 60
 cccctcctg tgccatcatg atcagcacct atgagttcgg caaaagcttc ttccagaggc 120
 tgaaccagga ccggcttctg ggcggtgaa aggggcaagg aggcaaggac cccgtctctc 180
 ccacggatgg ggagagggca ggaggagacc cagccaagtg ccttttcctc agcactgagg 240
 gagggggctt gtttcccttc cctcccggcg acaagctcca gggcagggct gtccctctgg 300
 gcggcccagc acttctcag acacaacttc ttctgtctgc tccagtcgtg gggatcatca 360
 cttaccacc cccaagttc aagaccaaata cttccagctg ccccttcgt gtttccctgt 420

```
<210> 388
<211> 520
<212> DNA
<213> Homo sapiens
```

```
<210> 389
<211> 365
<212> DNA
<213> Homo sapiens
```

```
<210> 390
<211> 221
<212> DNA
<213> Homo sapiens
```

<400>	390						
tgccctctcca	tctctggcccc	gacttctctctg	tcaggaaaagt	gggggatggac	cccatctgca	60	
tacacggntt	ctcatgggtg	tggaacatct	ctgcttgcg	tttcaggaag	gcctctggct	120	
gctctangag	ctctgancga	ntcgttgccc	cantntgaca	naaggaaagg	cgagacttat	180	
tcaaagtcta	qaqqgaqtqg	aggagttaag	gctggatttc	a		221	

```
<210> 391
<211> 325
<212> DNA
<213> Homo sapiens
```


<220>
 <221> misc_feature
 <222> (1)...(325)
 <223> n = A,T,C or G

<400> 391
 tggagcagggt ccgagggcct ccctagagcc tggggccgac tctgtgncga tgcangcttt 60
 ctctcgcgcc cagcctggag ctgctcctgg catctaccaa caatcagncg aggcgagcag 120
 tagccagggc actgctgcc aacagccagtc cnnataccat catgtnaccc ggtgngctct 180
 naanttngat ntccanagcc ctacccatcn tagttctgct ctcccaccgg ntaccagccc 240
 cactgcccag gaatcctaca gccagtagcc tgtcccagcg tctctaccta ccagtacgat 300
 gagacctccg gctactacta tgacc 325

<210> 392
 <211> 277
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(277)
 <223> n = A,T,C or G

<400> 392
 atattgttta actccttcct ttatatcttt taacattttc atggngaaaag gttcacatct 60
 agtctcactt nggcnagn gn ctcctacttg agtctcttcc ccggcctggn ccagtnagnaa 120
 antaccanga accgncatgn cttaanaacn nccgtggttn tgggttnntc aatgactgca 180
 tgcaagtgcac caccctgtcc actacgtgat gctgtaggat taaagtctca cagtgggcgg 240
 ctgaggatac agcgccgcgt cctgtgttgc tggggaa 277

<210> 393
 <211> 566
 <212> DNA
 <213> Homo sapiens

<400> 393
 actagtccag tgtggtggaa ttcgcggccg cgtcgacgga caggtcagct gtctggctca 60
 gtgatctaca ttctgaagtt gtctgaaaat gtcttcatga tttaaattcag cctaaacggt 120
 ttgccgggaa cactgcagag acaatgctgt gagtttccaa ccttagccca tctgcgggca 180
 gagaaggctc agtttgtcca tcagcattat catgatatac ggactgggta cttgggttaag 240
 gaggggtcta ggagatctgt cccttttaga gacaccttac ttataatgaa gtatttgga 300
 ggggtggttt caaaagtaga aatgtcctgt attccgatga tcatcctgta aacattttat 360
 catttattaa tcatccctgc ctgtgtctat tattatattc atatctctac gctggaaact 420
 ttctgcctca atgtttactg tgcctttgtt tttgctagtt tgtgttggtg aaaaaaaaaa 480
 cattctctgc ctgagtttta atttttgtcc aaagttattt taatctatac aattaaaagc 540
 ttttgcttat caaaaaaaaa aaaaaa 566

<210> 394
 <211> 384
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature

<222> (1)...(384)

<223> n = A,T,C or G

<400> 394

```

gaacatacat gtcccggcac ctgagctgca gtctgacatc atcgccatca cgggcctcgc 60
tgcaaatnng gaccggggcca aggctggact gctggagcgt gtgaaggagc tacaggccna 120
gcaggaggac cgggctttaa ggagttttaa gctgagtgtc actgtagacc ccaaatacca 180
tcccaagatt atcgggagaa agggggcagt aattacccaa atccggttgg agcatgacgt 240
gaacatccag tttcctgata aggacgatgg gaaccagccc caggaccaa ttaccatcac 300
agggtacgaa aagaacacag aagctgccag ggatgctata ctgagaattg tgggtgaact 360
tgagcagatg gtttctgagg acgt 384

```

<210> 395

<211> 399

<212> DNA

<213> Homo sapiens

<400> 395

```

ggcaaaactg tgtgacctca ataagacctc gcagatccaa ggtcaagtat cagaagtgac 60
tctgaccttg gactccaaga cctacatcaa cagcctggct atattagatg atgagccagt 120
tatcagaggt ttcattcattg cggaaattgt ggagtctaag gaaatcatgg cctctgaagt 180
attcacgtct ttccagtacc ctgagttctc tatagagttg cctaacacag gcagaattgg 240
ccagctactt gtctgcaatt gtatcttcaa gaataccctg gccatccctt tgactgacgt 300
caagttctct ttggaaaagcc tgggcatctc ctcaactacag acctctgacc atgggacggt 360
gcagcctggg gagaccatcc aatcccaaat aaaatgcac 399

```

<210> 396

<211> 403

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(403)

<223> n = A,T,C or G

<400> 396

```

tggagttntc agtgcaaaca agccataaag cttcagtagc aaattactgt ctcacagaaa 60
gacattttca acttctgctc cagctgctga taaaacaaat catgtgttta gcttgactcc 120
agacaaggac aacctgttcc ttcataactc tctagagaaa aaaaggagtt gttagtagat 180
actaaaaaaaa gtggatgaat aatctggata tttttcctaa aaagattcct tgaaacacat 240
taggaaaatg gagggcctta tgatcagaat gctagaatta gtccattgtg ctgaagcagg 300
gttttagggga gggagtggag gataaaaagaa ggaaaaaaag aagagtgaga aaacctattt 360
atcaaagcag gtgctatcac tcaatgttag gccctgctct ttt 403

```

<210> 397

<211> 100

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(100)

<223> n = A,T,C or G

<400> 397
 actagtnacag tgtggtggaa ttcgcggccg cgtcgaccta naanccatct ctatagcaaa 60
 tccatccccg ctcttggttg gtnacagaat gactgacaaa 100

<210> 398
 <211> 278
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(278)
 <223> n = A,T,C or G

<400> 398
 gcggccgcgt cgacagcagt tccgccagcg ctgcgccctg ggtggggatg tgctgcacgc 60
 ccacctggac atctggaagt cagcggcctg gatgaaagag cggacttcac ctggggcgat 120
 tcactactgt gcctcgacca gtgaggagag ctggaccgac agcgaggttg actcatcatg 180
 ctccgggcag cccatccacc tgtggcagtt cctcaaggag ttgctactca agccccacag 240
 ctatggccgc ttcattangt ggctcaacaa ggagaagg 278

<210> 399
 <211> 298
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(298)
 <223> n = A,T,C or G

<400> 399
 acggaggtgg aggaagcgnc cctgggatcg anaggatggg tcttgnatt gaccnctcn 60
 ggggtgccng catggagcgc atgggcgcgg gcctgggcca cggcatggat cgcgtgggct 120
 ccgagatcga gcgcattggc ctggtcatgg accgcattgg ctccgtggag cgcattggct 180
 ccggcattga gcgcattggc ccgctgggcc tcgaccacat ggccctccac attgancgca 240
 tgggccagac catggagcgc attggctctg gcgtggagcn catgggtgcc ggcatggg 298

<210> 400
 <211> 548
 <212> DNA
 <213> Homo sapiens

<400> 400
 acatcaacta cttcctcatt ttaaggatg gcagttccct tcatccctt ttcctgcctt 60
 gtacatgtac atgtatgaaa tttccttctc ttaccgaact ctctccacac atcacaaggt 120
 caaagaacca cagccttaga agggtaagag ggcaccctat gaaatgaaat ggtgatttct 180
 tgagtctctt ttttccacgt ttaaggggcc atggcaggac ttagagttgc gagttaagac 240
 tgcagagggc tagagaatta tttcatcacg gctttgaggc caccatgtc acttatcccg 300
 tataccctct caccatcccc ttgtctactc tgatgcccc aagatgcaac tgggcagcta 360
 gttggcccca taattctggg cctttgttgt ttgttttaat tacttgggca tcccaggaag 420
 ctttccagt atctcctacc atgggcccc ctcttggttg caagccctc ccaggccctg 480
 tccccagccc ctctgcccc agcccacccg cttgccttgg tgctcagccc tccattggg 540

agcaggtt

548

<210> 401

<211> 355

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(355)

<223> n = A,T,C or G

<400> 401

```

actgtttcca tgttatgttt ctacacattg ctacctcagt gtccttgga acttagcttt 60
tgatgtctcc aagtagtcca ccttcattta actctttgaa actgtatcat ctttgccaag 120
taagagtggg ggcctatttc agctgctttg acaaaatgac tggctcctga cttaacgttc 180
tataaatgaa tgtgctgaag caaagtgcc atgggtggcg cgaagaagan aaagatgtgt 240
tttgttttgg actctctgtg gtcccttcca atgctgnggg tttccaacca ggggaagggt 300
cccttttgca ttgccaagtg ccataaccat gagcactact ctaccatggn tctgc 355

```

<210> 402

<211> 407

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(407)

<223> n = A,T,C or G

<400> 402

```

atggggcaag ctggataaag aaccaagacc cactggagta tgctgtcttc aagaaaccca 60
tctcacatgc ggtggcatac ataggctcaa aataaaggaa tggagaaaaa tatttcaagc 120
aaatggaaaa cagaaaaaag caggtgttgc actcctactt tctgacaaaa cagactatgc 180
gaataaagat aaaaaagaga aggacattac aaaggtggtc ctgacctttg ataaatctca 240
ttgcttgata ccaacctggg ctgttttaat tgcccaaacc aaaaggataa tttgctgagg 300
ttgtggagct tctccctgac agagagtccc tgatctccca aaatttggtt gagatgtaag 360
gntgattttg ctgacaactc cttttctgaa gttttactca tttccaa 407

```

<210> 403

<211> 303

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(303)

<223> n = A,T,C or G

<400> 403

```

cagtatttat agccnaactg aaaagctagt agcaggcaag tctcaaatec aggcacccaa 60
tctaagcaa gagccatggc atggtgaaaa tgcaaaagga gagtctggcc aatctacaaa 120
tagagaacaa gacctactca gtcataaaca aaaaggcaga caccaacatg gatctcatgg 180
gggattggat attgtaatta tagagcagga agatgacagt gatcgtcatt tggcacaaca 240

```

006230"SEF560

tcttaacaac gaccgaaacc cattatTTac ataaacctcc attcggtaac catgttgaaa 300
gga 303

<210> 404
<211> 225
<212> DNA
<213> Homo sapiens

<400> 404
aagtgtact tttaaaaatt tagtggattt tgaaaattct tagaggaaag taaaggaaaa 60
attgttaatg cactcattta cctttacatg gtgaaagtcc tctcttgatc ctacaaacag 120
acattttcca ctcggtgttc catagtgtt aagtgtatca gatgtgttg gcatgtgaat 180
ctccaagtgc ctgtgtaata aataaagtat ctttatttca ttcatt 225

<210> 405
<211> 334
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(334)
<223> n = A,T,C or G

<400> 405
gagctgttat actgtgagtt ctactaggaa atcatcaaat ctgaggggtg tctggaggac 60
ttcaatacac ctcccccat agtgaatcag cttccagggg gtccagtccc tctccttact 120
tcatccccat cccatgccaa aggaagaccc tccctccttg gctcacagcc ttctctaggc 180
ttccagtgct ctccaggaca gagtgggtta tgttttcagc tccatccttg ctgtgagtgt 240
ctgggtgcgtg tgtgcctcca gcttctgctc agtgcttcat ggacagtgtc cagcccatgt 300
cactctccac tctctcanng tggatcccac ccct 334

<210> 406
<211> 216
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(216)
<223> n = A,T,C or G

<400> 406
tttcatacct aatgagggag ttganatnac atnnaaccag gaaatgcatg gatctcaang 60
gaaacaaaca cccaataaac tcggagtggc agactgacaa ctgtgagaca tgcacttgct 120
acnaaacaca aattttnatgt tgcacccttg tttctacacc tgtgggttat gacaaagaca 180
actgccaaag aatnttcaag aaggaggact gccant 216

<210> 407
<211> 413
<212> DNA
<213> Homo sapiens

<400> 407

006230 "GATGAGC"

```
<210> 408
<211> 183
<212> DNA
<213> Homo sapiens
```

```
<400> 408
ggagctngcc ctcaattcct ccatntctat gttancatat ttaatgtctt ttgnnattaa 60
tntttaacta gttaatcctt aaagggctan ntaatcctta actagtcctt ccattgtgag 120
cattatcctt ccagtattcn ccttctnttt tatttactcc ttcttggtta cccatgtact 180
ntt                                     183
```

```
<220>  
<221> misc_feature  
<222> (1)...(250)  
<223> n = A,T,C or G
```

```
<210> 410
<211> 306
<212> DNA
<213> Homo sapiens
```

```
<400> 410
ggctggtttg caagaatgaa atgaatgatt ctacagctag gacttaacct tgaaatggaa 60
agtctttgcaa tcccatattgc agqatccgtc tgtgcacatg cctctgtaga gaggcagcatt 120
```

```

cccagggacc ttggaacag ttggcactgt aagggtgcttg ctccccaaga cacatcctaa 180
aagggtgttg aatgggtgaaa accgcttcct tctttattgc cccttcttat ttatgtgaac 240
nactgggttg ctttttttgn atctttttta aactggaaag ttcaattgng aaaatgaata 300
tcntgc                                           306

```

```

<210> 411
<211> 261
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(261)
<223> n = A,T,C or G

```

```

<400> 411
agagatattn cttaggtnaa agttcataga gttcccatga actatatgac tggccacaca 60
ggatcttttg tatttaagga ttctgagatt ttgcttgagc aggattagat aaggctgttc 120
tttaaatgtc tgaaatggaa cagatttcaa aaaaaaaccc cacaatctag ggtgggaaca 180
aggaaggaaa gatgtgaata ggctgatggg caaaaaacca atttaccat cagttccagc 240
cttctctcaa gngaggcaa a                                           261

```

```

<210> 412
<211> 241
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(241)
<223> n = A,T,C or G

```

```

<400> 412
gttcaatgtt acctgacatt tctacaacac cccactcacc gatgtattcg ttgccagtg 60
ggaacatacc agcctgaatt tggaaaaaat aattgtgttt cttgccagg aaatactacg 120
actgactttg atggctccac aaacataacc cagtgtaaaa acagaagatg tggaggggag 180
ctgggagatt tctactggta cattgaattc caaaactacc cangcaatta cccagccaac 240
a                                           241

```

```

<210> 413
<211> 231
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(231)
<223> n = A,T,C or G

```

```

<400> 413
aactcttaca atccaagtga ctcatctgtg tgcttgaatc ctttccactg tctcatctcc 60
ctcatccaag tttctagtac cttctctttg ttgtgaagga taatcaaact gaacaacaaa 120
aagtttactc tctctatttg gaacctaaaa actctcttct tcttgggtct gagggctcca 180
agaatccttg aatcanttct cagatcattg gggacaccan atcaggaacc t                                           231

```

<210> 414
 <211> 234
 <212> DNA
 <213> Homo sapiens

<400> 414
 actgtccatg aagcactgag cagaagctgg aggcacaacg caccagacac tcacagcaag 60
 gatggagctg aaaacataac ccactctgtc ctggaggcac tgggaagcct agagaaggct 120
 gtgagccaag gagggagggt cttcctttgg catgggatgg ggatgaagta aggagaggga 180
 ctggaccccc tggaagctga ttcactatgg ggggagggtg attgaagtcc tcca 234

<210> 415
 <211> 217
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(217)
 <223> n = A,T,C or G

<400> 415
 gcataggatt aagactgagt atcttttcta cattctttta actttctaag gggcacttct 60
 caaaacacag accaggtagc aaatctccac tgctctaagg ntctcaccac cacttttctca 120
 cacctagcaa tagtagaatt cagtcctact tctgaggcca gaagaatggg tcagaaaaat 180
 antggattat aaaaaataac aattaagaaa aataatc 217

<210> 416
 <211> 213
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(213)
 <223> n = A,T,C or G

<400> 416
 atgcatatnt aaagganact gcctcgcttt tagaagacat ctggnetgct ctctgcatga 60
 ggcacagcag taaagctctt tgattcccag aatcaagaac tctccccttc agactattac 120
 cgaatgcaag gtgggttaatt gaaggccact aattgatgct caaatagaag gatattgact 180
 atattggaac agatggagtc tctactacaa aag 213

<210> 417
 <211> 303
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(303)
 <223> n = A,T,C or G

<400> 417

```

nagtcttcag gcccatcagg gaagttcaca ctggagagaa gtcatacata tgtactgtat 60
gtgggaaagg ctttactctg agttcaaate ttcaagccca tcagagagtc cactactggag 120
agaagccata caaatgcaat gagtgtggga agagcttcag gagggattcc cattatcaag 180
ttcatctagt ggtccacaca ggagagaaac cctataaatg tgagatatgt gggaagggct 240
tcantcaaag ttcgtatctt caaatccatc ngaaggncca cagtatanan aaacctttta 300
agt 303

```

<210> 418

<211> 328

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(328)

<223> n = A,T,C or G

<400> 418

```

tttttggcgg tgggtgggca gggacgggac angagtctca ctctgttgcc caggctggag 60
tgcacaggca tgatctcggc tcaactacaac ccctgcctcc catgtccaag cgattcttgt 120
gcctcagcct tcctgttagc tagaattaca ggcacatgcc accacaccca gctagttttt 180
gtatttttag tagagacagg gtttcacccat gttggccagg ctggtctcaa actcctnacc 240
tcagnggtca ggctggcttc aaactcctga cctcaagtga tctgcccacc tcagcctccc 300
aaagtgctan gattacaggc cgtgagcc 328

```

<210> 419

<211> 389

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(389)

<223> n = A,T,C or G

<400> 419

```

cctcctcaag acggcctgtg gtccgcctcc cggcaaccaa gaagcctgca gtgccatag 60
acccttgagc catggactgg agcctgaaag gcagcgtaca ccctgctcct gatcttgtgt 120
cttgtttctt ctctgtggct ccattcatag cacagttgtt gcaactgagga ttgtgcaggc 180
cgagcaaggc caagctggct caaagagcaa ccagtcaact ctgccacggg gtgccaggca 240
ccggttctcc agccaccaac ctcaactcgt cccgcaaagt gcacatcagt tcttctaccc 300
taaaggtagg accaaagggc atctgtcttt ctgaagtcct ctgctctatc agccatcacg 360
tggcagccac tcnggctgtg tcgacgcgg 389

```

<210> 420

<211> 408

<212> DNA

<213> Homo sapiens

<400> 420

```

gttctctcta actcctgcca gaaacagctc tctcaacat gagagctgca cccctcctcc 60
tggccagggc agcaagcctt agccttggct tcttgtttct gctttttttc tggctagacc 120
gaagtgtact agccaaggag ttgaagtgtt tgacttttgt gtttcggcat ggagaccgaa 180

```

006230 "3E2T5960

```
<210> 421
<211> 352
<212> DNA
<213> Homo sapiens
```

<400>	421						
gctcaaaaat	cttttttactg	atnggcacatg	ctacacaatc	attgactatt	acggaggcca	60	
gaggagaatg	aggcctggcc	tgggagccct	gtgcctacta	naagcacatt	agattatcca	120	
ttcaactgaca	gaacagggtct	tttttggtgc	cttcttctcc	accacnatat	acttgcagtc	180	
ctcctttcttg	aagattcttt	ggcagttgtc	tttgtcataa	cccacaggtg	tgaaaacaag	240	
ggtgcaacct	gaaattttctg	tttcgtagca	agtgcacatg	tcacaagttg	gcangtctgc	300	
cactcqaagt	ttattggaatg	tttgttttcc	tttgatccca	tgcatttctc	gg	352	

<400>	422						
atgccaccat	gctggcaatg	cagcggggcgg	tcgaaggcct	gcataatccag	ccaagctgg	60	
cgatgatcga	cggcaaccgt	tgcccgaagt	tgccgatgcc	agccgaagcg	gtggtcaagg	120	
gcgatagcaa	ggtgcccggcg	atcgccggcgg	cgtcaatcct	ggccaagggtc	agccgtgatc	180	
gtgaaatggc	agctgtcgaa	ttgatctacc	cgggttatgg	catcggcggg	cataagggct	240	
atccgacacc	ggtgcacctc	gaagccttgc	agcggtctgg	gccgacgcgc	atcacccgac	300	
gcttcttcgc	ccggtacggc	tggcctatga	aaattat			337	

```
<220>
<221> misc_feature
<222> (1)...(310)
<223> n = A,T,C or G
```

```
<400> 423
gctcaaaaat ctttttactg atatggcatg gctacacaat cattgactat tagaggccag 60
aggagaatga ggcctggcct gggagccctg tgctactan aagcncatta gattatccat 120
tcactgacag aacagggtctt ttttgggtcc ttcttctcca ccacgatata cttgcagtcc 180
tccttcttga agattctttg gcagttgtct ttgtcataac ccacaggtgt anaaacaagg 240
gtgcaacatg aaatttctgt ttcgtagcaa gtgcatgtct cacagttgtc aagtctgccc 300
tccgagttta                                     310
```

<210> 424
 <211> 370
 <212> DNA
 <213> Homo sapiens
 <220>
 <221> misc_feature
 <222> (1)...(370)
 <223> n = A,T,C or G

<400> 424
 gctcaaaaat ctttttactg ataggcatgg ctacacaatc attgactatt agaggccaga 60
 ggagaatgag gcctggcctg ggagccctgt gcctactaga agcacattag attatccatt 120
 cactgacaga acaggtcttt ttggggctct tcttctccac cacgatatac ttgcagtcct 180
 ccttcttgaa gattctttgg cagttgtctt tgtcataacc cacaggtgta gaaacatcct 240
 gggtgaatct cctggaactc cctcattagg tatgaaatag catgatgcat tgcataaagt 300
 cacgaaggtg gcaaagatca caacgctgcc cagganaaca ttcattgtga taagcaggac 360
 tccgtcgacg 370

<210> 425
 <211> 216
 <212> DNA
 <213> Homo sapiens
 <220>
 <221> misc_feature
 <222> (1)...(216)
 <223> n = A,T,C or G

<400> 425
 aattgctatn ntttatcttg ccaactcaaaa taattaccaa aaaaaaaaaa tnttaaatga 60
 taacaacnca acatcaaggc aaananaaca ggaatggntg actntgcata aatnggccga 120
 anattatcca ttatnttaag gggtgacttc aggntacagc acacagacaa acatgcccag 180
 gaggnnttca ggaccgctcg atgtnttntg aggagg 216

<210> 426
 <211> 596
 <212> DNA
 <213> Homo sapiens

<400> 426
 cttccagtga ggataaccct gttgccccgg gccgaggttc tccattaggc tctgattgat 60
 tggcagtcag tgatggaagg gtgttctgat cattccgact gcccgaaggg tcgctggcca 120
 gctctctgtt ttgctgagtt ggcagtagga cctaatttgt taattaagag tagatgggtga 180
 gctgtccttg tattttgatt aacctaattg ccttcccagc acgactcgga ttcagctgga 240
 gacatcacgg caacttttaa tgaaatgatt tgaagggcca ttaagaggca cttcccgtta 300
 ttaggcagtt catctgcact gataacttct tggcagctga gctggctgga gctgtggccc 360
 aaacgcacac ttggcctttg gttttgagat acaactctta atcttttagt catgcttgag 420
 ggtggatggc cttttcagct ttaacccaat ttgcaactgc ttggaagtgt agccaggaga 480
 atacactcat atactcgtgg gcttagaggc cacagcagat gtcattggtc tactgcctga 540
 gtcccgcgtg tcccatccca ggaccttcca tcggcgagta cctgggagcc cgtgct 596

<210> 427
 <211> 107

006290" 9E2T5960

<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(107)
<223> n = A,T,C or G

<400> 427
gaagaattca agttaggttt attcaaaggg cttacngaga atcctanacc caggncaccag 60
cccgaggagca gccttanaga gctcctgttt gactgcccgg ctcagng 107

<210> 428
<211> 38
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(38)
<223> n = A,T,C or G

<400> 428
gaatttcena anaangactt tattcactat tttacatt 38

<210> 429
<211> 544
<212> DNA
<213> Homo sapiens

<400> 429
ctttgctgga cggaataaaa gtggacgcaa gcatgacctc ctgatgaggg cgctgcattt 60
attgaagagc ggctgcagcc ctgcggttca gattaaaatc cgagaattgt atagacgccg 120
atatccacga actcttgaag gactttctga tttatccaca atcaaatacat cggttttcag 180
tttggtggtt ggctcatcac ctgtagaacc tgacttggcc gtggctggaa tccactcgtt 240
gccttcactc tcagttacac ctcactcacc atcctctcct gttggttctg tgctgcttca 300
agatactaag cccacatttg agatgcagca gccatctccc ccaattcctc ctgtccatcc 360
tgatgtgcag ttaaaaaatc tgccttttta tgatgtcctt gatgttctca tcaagcccac 420
gagtttagtt caaagcagta ttcagcgatt tcaagagaag ttttttattt ttgctttgac 480
acctcaacaa gttagagaga tatgcatatc cagggatttt ttgccaggtg gtaggagaga 540
ttat 544

<210> 430
<211> 507
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(507)
<223> n = A,T,C or G

<400> 430
cttatcncaa tggggctccc aaacttggct gtgcagtgga aactccgggg gaattttgaa 60

```

gaacactgac acccatcttc ccccccgaca ctctgattta attgggctgc agtgagaaca 120
gagcatcaat ttaaaaagct gcccagaatg ttntcctggg cagcgttgtg atctttgccn 180
ccttcgtgac tttatgcaat gcatcatgct atttcatacc taatgaggga gttccaggag 240
attcaaccag gatgtttcta cncctgtggg ttatgacaaa gacaactgcc aaagaatntt 300
caagaaggag gactgcaagt atatcgtggg ggagaagaag gacccaaaaa agacctgttc 360
tgtcagtgaa tggataatct aatgtgcttc tagtaggcac agggctccca ggccaggcct 420
cattctcctc tggcctctaa tagtcaatga ttgtgtagcc atgcctatca gtaaaaagat 480
ttttgagcaa aaaaaaaaaa aaaaaaaa 507

```

<210> 431

<211> 392

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(392)

<223> n = A,T,C or G

<400> 431

```

gaaaattcag aatggataaa aacaaatgaa gtacaaaata tttcagattt acatagcgat 60
aaacaagaaa gcacttatca ggaggactta caaatggaag tacactctan aaccatcatc 120
tatcatggct aaatgtgaga ttagcacagc tgtattatth gtacattgca aacacctaga 180
aagagatggg aaacaaaatc ccaggagttt tgtgtgtgga gtccctgggtt ttccaacaga 240
catcattcca gcattctgag attagggnga ttggggatca ttctggagtt ggaatgttca 300
acaaaagtga tgttgtagg taaaatgtac aacttctgga tctatgcaga cattgaaggt 360
gcaatgagtc tggcttttac tctgctgttt ct 392

```

<210> 432

<211> 387

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(387)

<223> n = A,T,C or G

<400> 432

```

ggtatccta cataatcaaa tatagctgta gtacatgttt tcattggngt agattaccac 60
aaatgcaagg caacatgtgt agatctcttg tcttattott ttgtctataa tactgtattg 120
ngtagtccaa gctctcgna gtccagccac tngaaacat gctcccttta gattaacctc 180
gtggacnctn ttgttgnatt gtctgaactg tagngccctg tattttgctt ctgtctgnga 240
attctgttgc ttctggggca tttccttgng atgcagagga ccaccacaca gatgacagca 300
atctgaattg ntccaatcac agctgcgatt aagacatact gaaatcgtac aggaccggga 360
acaacgtata gaacactgga gtccttt 387

```

<210> 433

<211> 281

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(281)

<223> n = A,T,C or G

<400> 433

```
ttcaactagc anagaanact gcttcagggn gtgtaaaatg aaaggcttcc acgcagttat 60
ctgattaaag aacactaaga gagggacaag gctagaagcc gcaggatgtc tacactatag 120
caggcnctat ttgggttggc tggaggagct gtggaaaaca tggagagatt ggcgctggag 180
atcgccgtgg ctattcctcn ttgntattac accagnagg ntctctgtnt gccactggg 240
tnnaaaaccg ntatacaata atgatagaat aggacacaca t 281
```

<210> 434

<211> 484

<212> DNA

<213> Homo sapiens

<400> 434

```
ttttaaaata agcatttagt gctcagtcct tactgagtag tctttctctc cctcctctg 60
aatttaattc tttcaacttg caatttgcaa ggattacaca tttcactgtg atgtatattg 120
tggtgcaaaa aaaaaaaagt gtctttgttt aaaattactt ggtttgtaga tccatcttgc 180
tttttcccca ttggaactag tcattaaccc atctctgaac tggtagaaaa acatctgaag 240
agctagtcta tcagcatctg acaggtgaat tggatgggtc tcagaaccat ttcaccaga 300
cagcctgttt ctatcctgtt taataaaatta gtttggttgc tctacatgca taacaaaccc 360
tgctccaatc tgtcacataa aagtctgtga cttgaagttt agtcagcacc cccaccaaac 420
tttatttttc tatgtgtttt ttgcaacata tgagtgtttt gaaaataaag taccatgtc 480
ttta 484
```

<210> 435

<211> 424

<212> DNA

<213> Homo sapiens

<400> 435

```
gcgcgcgtca gagcagggtca ctttctgcct tccacgtcct ccttcaagga agccccatgt 60
gggtagcttt caatatcgca ggttcttact cctctgcctc tataagctca aaccaccaa 120
cgatcgggca agtaaacccc ctccctcgcc gacttcggaa ctggcgagag ttcagcgag 180
atgggcctgt ggggaggggg caagatagat gagggggagc ggcattggtc ggggtgacct 240
cttgagaga ggaaaaaggc cacaagaggg gctgccaccg ccactaacgg agatggccct 300
ggtagagacc tttgggggtc tggaacctct ggactcccca tgctctaact cccacactct 360
gctatcagaa acttaaactt gaggattttc tctgtttttc actcgcaata aattcagagc 420
aaac 424
```

<210> 436

<211> 667

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(667)

<223> n = A,T,C or G

<400> 436

```
accttgggaa nactctcaca atataaaggg tcgtagactt tactccaaat tccaaaaagg 60
tcttgcccat gtaatcctga aagttttccc aaggtagcta taaaatcctt ataaggtgct 120
```

```

agcctcttct ggaattcctc tgatttcaaa gtctcactct caagttcttg aaaacgaggg 180
cagttcctga aaggcaggta tagcaactga tcttcagaaa gaggaactgt gtgcaccggg 240
atgggctgcc agagtaggat aggattccag atgctgacac cttctggggg aaacagggct 300
gccaggtttg tcatagcact catcaaagtc cgggtcaacgt ctgtgcttcg aatataaacc 360
tgttcatgtt tataggactc attcaagaat tttctatata tctttcttat atactctcca 420
agttcataat gctgctccat gcccagctgg gtgagttggc caaatccttg tggccatgag 480
gattccttta tggggtcagt gggaaagggt tcaatgggac ttcgggtctcc atgccgaaac 540
accaaagtca caaacttcaa ctccctgggt agtacacttc ggtctagcca gaaaaaagc 600
agaaacaaga agccaaggct aaggcttgct gccctgccag gaggaggggt gcagctctca 660
tgttgag                                         667

```

<210> 437

<211> 693

<212> DNA

<213> Homo sapiens

<400> 437

```

ctacgtctca accctcattt ttaggtaagg aatcttaagt ccaaagatat taagtgactc 60
acacagccag gtaaggaaag ctggattggc acactaggac tctaccatac cgggttttgt 120
taaagctcag gttaggaggc tgataagctt ggaaggaaact tcagacagct ttttcagatc 180
ataaaagata attcttagcc catgttcttc tccagagcag acctgaaatg acagcacagc 240
aggtaactct ctattttcac cctcttggt tctactctct ggcagtcaga cctgtgggag 300
gccatgggag aaagcagctc tctggatgtt tgtacagatc atggactatt ctctgtggac 360
catttctcca ggttacccta ggtgtcacta ttgggggggac agccagcatc tttagctttc 420
atgtgagttt ctgtctgtct tcagtagagg aaacttttgc tcttcacact tcacatctga 480
acacctaact gctgttgctc ctgaggtggg gaaagacaga tatagagctt acagtattta 540
tcctatttct aggcaactgag ggctgtgggg taccttggtg tgccaaaaca gatcctgttt 600
taaggacatg ttgcttcaga gatgtctgta actatctggg ggctctgttg gctctttacc 660
ctgcatcatg tgctctcttg gctgaaaatg acc                                         693

```

<210> 438

<211> 360

<212> DNA

<213> Homo sapiens

<400> 438

```

ctgcttatca caatgaatgt tctcctgggc agcgttgtga tctttgccac cttcgtgact 60
ttatgcaatg catcatgcta tttcatacct aatgagggag ttccaggaga ttcaaccagg 120
atgtttctac acctgtgggt tatgacaaag acaactgcc aagaatcttc aagaaggagg 180
actgcaagta tatctgggtg agaagaagga cccaaaaaag acctgttctg tcagtgaatg 240
gataatctaa tgtgcttcta gtaggcacag ggctcccagg ccaggcctca ttctcctctg 300
gcctctaata gtcaataatt gtgtagccat gcctatcagt aaaaagattt ttgagcaaac 360

```

<210> 439

<211> 431

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(431)

<223> n = A,T,C or G

<400> 439

```

gttcctnnta actcctgcc aaaaacagctc tcttcaacat gagagctgca cccctcctcc 60
tggccagggc agcaagcctt agccttggct tcttgtttct gctttttttc tggctagacc 120
gaagtgtact agccaaggag ttgaagtttg tgacttttgg gtttcggcat ggagaccgaa 180
gtcccattga cacctttccc actgacccca taaaggaatc ctcattggcca caaggatttg 240
gccaaactcac ccagctgggc atggagcagc attatgaact tggagagtat ataagaaaga 300
gatatagaaa attccttgaat gagtcctata aacatgaaca ggtttatatt cgaagcacag 360
acgttgaccg gactttgatg agtgctatga caaacctggc agcccgctga cgcggccgcg 420
aatttagtag t 431

```

<210> 440

<211> 523

<212> DNA

<213> Homo sapiens

<400> 440

```

agagataaag cttaggtcaa agttcataga gttcccatga actatatgac tggccacaca 60
ggatcttttg tatttaagga ttctgagatt ttgcttgagc aggattagat aaggctgttc 120
tttaaatgtc tgaaatggaa cagatttcaa aaaaaaaccc cacaatctag ggtgggaaca 180
aggaaggaaa gatgtgaata ggctgatggg caaaaaacca atttaccat cagttccagc 240
cttctctcaa ggagaggcaa agaaaggaga tacagtggag acatctggaa agttttctcc 300
actggaaaac tgctactatc tgtttttata tttctgttaa aatatatgag gctacagaac 360
taaaaaattaa aacctctttg tgtcccttgg tcttggaaaca tttatgttcc ttttaaagaa 420
acaaaaatca aactttacag aaagatttga tgtatgtaac acatatagca gctcttgaag 480
tatatatatc atagcaaata agtcatctga tgagaacaag cta 523

```

<210> 441

<211> 430

<212> DNA

<213> Homo sapiens

<400> 441

```

gttcctccta actcctgcc aaaaacagctc tcttcaacat gagagctgca cccctcctcc 60
tggccagggc agcaagcctt agccttggct tcttgtttct gctttttttc tggctagacc 120
gaagtgtact agccaaggag ttgaagtttg tgacttttgg gtttcggcat ggagaccgaa 180
gtcccattga cacctttccc actgacccca taaaggaatc ctcattggcca caaggatttg 240
gccaaactcac ccagctgggc atggagcagc attatgaact tggagagtat ataagaaaga 300
gatatagaaa attccttgaat gagtcctata aacatgaaca ggtttatatt cgaagcacag 360
acgttgaccg gactttgatg agtgctatga caaacctggc agcccgctga cgcggccgcg 420
aatttagtag 430

```

<210> 442

<211> 362

<212> DNA

<213> Homo sapiens

<400> 442

```

ctaaggaatt agtagtgctt ccatcacttg tttggagtgt gctattctaa aagattttga 60
tttcctggaa tgacaattat attttaactt tgggtggggg aagagttata ggaccacagt 120
cttcacttct gatacttgta aattaatctt ttattgcact tgttttgacc attaatgtat 180
atgttttagaa atggtcattt tacggaaaaa ttagaaaaat tctgataata gtgcagaata 240
aatgaattaa tgttttactt aatttatatt gaactgtcaa tgacaaataa aaattctttt 300
tgattatatt ttgttttcat ttaccagaat aaaaactaag aattaaaagt ttgattacag 360
tc 362

```



```
<220>
<221> misc_feature
<222> (1)...(624)
<223> n = A,T,C or G
```

```
<210> 444
<211> 425
<212> DNA
<213> Homo sapiens
```

```
<400> 444
gcacatcatt nntcttgc at tctttgagaa taagaagatc agtaaatagt tcagaagtgg 60
gaagctttgt ccaggcctgt gtgtgaaccc aatgttttgc ttagaaatag aacaagtaag 120
ttcattgcta tagcataaca caaaatttgc ataagtgggtg gtcagcaaat ccttgaatgc 180
tgcttaatgt gagaggttgg taaaatcctt tgtgcaacac tctaactccc tgaatgtttt 240
gctgtgctgg gacctgtgca tgccagacaa ggccaagctg gctgaaaagag caaccagcca 300
cctctgcaat ctgccacctc ctgctggcag gatttgtttt tgcactctgt gaagagccaa 360
ggaggcacca gggcataagt gagtagactt atggtcgacg cggccgcgaa tttagtagta 420
qtaga
425
```

```
<220>  
<221> misc_feature  
<222> (1)...(414)  
<223> n = A,T,C or G
```

<400> 445

```

catgtttatg nttttggatt actttgggca cctagtgttt ctaaactcgtc tatcattctt 60
ttctgttttt caaaagcaga gatggccaga gtctcaacaa actgtatctt caagtctttg 120
tgaaattctt tgcattgtggc agattatttg atgtagtttc ctttaactag catataaatc 180
tgggtgtgtt cagataaatg aacagcaaaa tgtggtggaa ttaccatttg gaacattgtg 240
aatgaaaaat tgtgtctcta gattatgtaa caaataacta tttcctaacc attgatcttt 300
ggatttttat aatcctactc acaaagtact aggccttctc tcttgtattt tgaagcagtg 360
tgggtgctgg attgataaaa aaaaaaaaaa tgcagcgggc cgcaattta gtag 414

```

<210> 446

<211> 631

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(631)

<223> n = A,T,C or G

<400> 446

```

acaaattaga anaaagtgcc agagaacacc acataccttg tccggaacat tacaatggct 60
tctgcatgca tgggaagtgt gagcattcta tcaatatgca ggagccatct tgcaggtgtg 120
atgctgggta tactggacaa cactgtgaaa aaaaggacta cagtgttcta tacgttggtc 180
ccggtcctgt acgatttcag tatgtcttaa tgcagctgt gattggaaca attcagattg 240
ctgtcatctg tgtggtggtc ctctgcatca caagggccaa actttaggta atagcattgg 300
actgagattt gtaaaccttc caaccttcca ggaaatgccc cagaagcaac agaattcaca 360
gacagaagca aaatacaggg cactacagtt cagacaatac aacaagagcg tccacgaggt 420
taatctaaag ggagcatgtt tcacagtggc tggactaccg agagcttgga ctacacaata 480
cagtattata gacaaaagaa taagacaaga gatctacaca tgttgcttg catttggtgt 540
aatctacacc aatgaaaaca tgtactacag ctatatgtga ttatgtatgg atatatttga 600
aatagtatac attgtcttga tgtttttct g 631

```

<210> 447

<211> 585

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(585)

<223> n = A,T,C or G

<400> 447

```

ccttgggaaa antntcacia tataaagggt cgtagacttt actccaaatt ccaaaaagggt 60
cctggccatg taatcctgaa agttttccca aggtagctat aaaatcctta taagggtgca 120
gcctcttctg gaattcctct gatttcaaag tctcactctc aagttcttga aaacgagggc 180
agttcctgaa aggcaggtat agcaactgat cttcagaaaag aggaactgtg tgcaccggga 240
tgggctgcca gagtaggata ggattccaga tgcagacacc ttctggggga aacagggctg 300
ccaggtttgt catagcactc atcaaagtcc ggtcaacgtc tgtgcttcga atataaacct 360
gttcatgttt ataggactca ttcaagaatt ttctatatct ctttcttata tactctccaa 420
gttcataatg ctgctccatg cccagctggg tgagttggcc aaatccttgt ggccatgagg 480
attcctttat ggggtcagtg ggaaagggtg caatgggact tgggtctcca tgccgaaaca 540
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<210> 448

<211> 93
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(93)
 <223> n = A,T,C or G

<400> 448
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 ggctccctag tgccttgag agganggggc tag 93

<210> 449
 <211> 706
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(706)
 <223> n = A,T,C or G

<400> 449
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 ttctgancac cgaactgacc atgccagccc tgccgatggg cctccatggc tccctagtgc 120
 cctggagagg aggtgtctag tcagagagta gtccctggaag gtggcctctg ngaggagcca 180
 cggggacagc atcctgcaga tggtcgggcg cgctccattc gccattcagg ctgcgcaact 240
 gttgggaagg gcgatcggtg cgggcctctt cgctattacg ccagctggcg aaagggggat 300
 gtgctgcaag gcgattaaat tgggtaacgc caggggtttc ccagtcncca cggtgtaaaa 360
 cgacggccag tgaattgaat ttaggtgacn ctatagaaga gctatgacgt cgcattgcacg 420
 cgtacgtaag cttggatcct cttagagcggc cgctactac tactaaattc gcggccgcgt 480
 cgacgtggga tcncactga gagagtggag agtgacatgt gctggacnct gtccatgaag 540
 cactgagcag aagctggagg cacaacgcnc cagacactca cagctactca ggaggctgag 600
 aacaggttga acctgggagg tggaggttgc aatgagctga gatcaggccn ctgcncccca 660
 gcatggatga cagagtgaat ctccatctta aaaaaaaaaa aaaaaa 706

<210> 450
 <211> 493
 <212> DNA
 <213> Homo sapiens

<400> 450
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 acagttttta aaggtaaaac aacataaaaa gaaatatcct atagtggaaa taagagagtc 120
 aaatgaggct gagaacttta caaagggatc ttacagacat gtcgccaaata tcaactgcatg 180
 agcctaagta taagaacaac ctttggggag aaaccatcat ttgacagtga ggtacaattc 240
 caagtcagggt agtgaaatgg gtggaattaa actcaaatta atcctgccag ctgaaacgca 300
 agagacactg tcagagagtt aaaaagttag ttctatccat gaggtgattc cacagtcttc 360
 tcaagtcaac acatctgtga actcacagac caagttctta aaccactgtt caaactctgc 420
 tacacatcag aatcacctgg agagctttac aaactcccat tgccgagggt cgacgcggcc 480
 gcgaatttag tag 493

<210> 451

005230"9215950

<211> 501
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(501)
 <223> n = A,T,C or G

<400> 451
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 ctcttcgcta ttacgccagc tggcgaaagg gggatgtgct gcaaggcgat taagttgggt 120
 aacgccaggg ttttcccagt cncgacgttg taaaacgacg gccagtgaat tgaatttagg 180
 tgacnctata gaagagctat gacgtcgcat gcacgcgtac gtaagcttgg atcctctaga 240
 gcggccgcct actactacta aattcgcggc cgcgtcgacg tgggatccnc actgagagag 300
 tggagagtga catgtgctgg acnctgtcca tgaagcactg agcagaagct ggaggcacia 360
 cgcncagac actcacagct actcaggagg ctgagaacag gttgaacctg ggaggtggag 420
 gttgcaatga gctgagatca ggcncctgcn cccagcatg gatgacagag tgaaactcca 480
 tcttaaaaaa aaaaaaaaaa a 501

<210> 452
 <211> 51
 <212> DNA
 <213> Homo sapiens

<220>
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 <222> (1)...(51)
 <223> n = A,T,C or G

<400> 452
 agacgggtttc accnttacaa cnccttttag gatgggnntt ggggagcaag c 51

<210> 453
 <211> 317
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(317)
 <223> n = A,T,C or G

<400> 453
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 acatctgaag agctagtcta tcagcatctg gcaagtgaat tggatggttc tcagaaccat 120
 ttcacccana cagcctgttt ctatcctgtt taataaatta gtttgggttc tctacatgca 180
 taacaaaccc tgctccaatc tgtcacataa aagtctgtga cttgaagttt antcagcacc 240
 cccaccaaac tttatttttc tatgtgtttt ttgcaacata tgagtgtttt gaaaataagg 300
 taccatgtc tttatta 317

<210> 454
 <211> 231
 <212> DNA

<213> Homo sapiens

<400> 454

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ttcgaggtag aatcaactct cagagtgtag tttccttcta tagatgagtc agcattaata 60
taagccacgc cacgctcttg aaggagtctt gaattctcct ctgctcactc agtagaacca 120
agaagaccaa attcttctgc atcccagctt gcaaacaaaa ttgttcttct aggtctccac 180
ccttcctttt tcagtgttcc aaagctcctc acaatttcat gaacaacagc t 231
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<210> 455

<211> 231

<212> DNA

<213> Homo sapiens

<400> 455

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taccaaagag ggcataataa tcagtctcac agtaggggttc accatcctcc aagtgaaaaa 60
cattgttccg aatgggcttt ccacaggcta cacacacaaa acaggaaaca tgccaagttt 120
gtttcaacgc attgatgact tctccaagga tcttcctttg gcatcgacca cattcagggg 180
caaagaattt ctcatagcac agctcacaat acagggtccc tttctcctct a 231
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<210> 456

<211> 231

<212> DNA

<213> Homo sapiens

<400> 456

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ttggcaggta cccttacaata gaagacacca taccttatgc gttattaggt ggaataatca 60
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tgcactcaaa ttcctttatc aggaataact acatagccac tatttacaata gccattggaa 180
cctttttatt tgggtgcagct gctagtcagt ccctgactga cattgccaag t 231
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<210> 457

<211> 231

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(231)

<223> n = A,T,C or G

<400> 457

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cgaggtagcc aggggtctga aaatctctnn tttantagtc gatagcaaaa ttgttcatca 60
gcattcctta atatgatctt gctataatta gatttttctc cattagagtt catacagttt 120
tatttgattt tattagcaat ctctttcaga agacccttga gatcattaag ctttgtatcc 180
agttgtctaa atcgatgcct catttcctct gaggtgtcgc tggcttttgt g 231
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<210> 458

<211> 231

<212> DNA

<213> Homo sapiens

<400> 458

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aggtctgggt cccccactt cactccctct ctactctctc taggactggg ctgggccaag 60
agaagagggg tgggttagga agccgttagg acctgaagcc ccacctcta ccttccttca 120
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acaccctaac cttgggtaac agcatttgga attatcattt gggatgagta gaatttccaa 180
 ggtcctgggt taggcatttt ggggggcccag accccaggag aagaagattc t 231

<210> 459

<211> 231

<212> DNA

<213> Homo sapiens

<400> 459

ggtaccgagg ctcgctgaca cagagaaacc ccaacgcgag gaaaggaatg gccagccaca 60
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 gccctgcact gttttccctc caccacagcc atcctgtccc tcattggctc tgtgctttcc 180
 actatacaca gtcaccgtcc caatgagaaa caagaaggag caccctccac a 231

<210> 460

<211> 231

<212> DNA

<213> Homo sapiens

<400> 460

gcaggtataa catgctgcaa caacagatgt gactaggaac ggccggtgac atggggaggg 60
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 cccacctccc cacacgcaca cgccagcct ggagcccaca gaagggtcct cctgcagcca 180
 gtggagcttg gtccagcctc cagtccaccc ctaccaggct taaggataga a 231

<210> 461

<211> 231

<212> DNA

<213> Homo sapiens

<400> 461

cgaggtttga gaagctctaa tgtgcagggg agccgagaag caggcggcct agggaggggtc 60
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 gtggggttca gtgaggagtg ggaaattggt tcagcagaac caagccgttg ggtgaataag 180
 agggggattc catggcactg atagagccct atagtctcag agctgggaat t 231

<210> 462

<211> 231

<212> DNA

<213> Homo sapiens

<400> 462

aggtaccctc attgtagcca tgggaaaatt gatgttcagt ggggatcagt gaattaaatg 60
 gggatcatgca agtataaaaa ttaaaaaaaaa aagacttcat gccaatctc atatgatgtg 120
 gaagaactgt tagagagacc aacagggtag tgggttagag attccagag tcttacattt 180
 tctagaggag gtatttaatt tcttctcact catccagtgt tgtatttagg a 231

<210> 463

<211> 231

<212> DNA

<213> Homo sapiens

<400> 463

tactccagcc tgggtacaga gcgagaccct atcaccgccc cccacccccc caaaaaaaaa 60

actgagtaga caggtgtcct cttggcatgg taagtcttaa gtccccctccc agatctgtga 120
 catttgacag gtgtcttttc ctctggacct cgggtgtcccc atctgagtga gaaaaggcag 180
 tggggagggtg gatcttccag tcgaagcggg atagaagccc gtgtgaaaag c 231

<210> 464

<211> 231

<212> DNA

<213> Homo sapiens

<400> 464

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 aaggacatca catatgaaga atgtttaagt tggagggtggc aacgtgaatt gcaaacaggg 120
 cctgcttcag tgactgtgtg cctgtagtcc cagctactcg ggagtctgtg tgaggccagg 180
 ggtgccagcg caccagctag atgctctgta acttctaggc cccattttcc c 231

<210> 465

<211> 231

<212> DNA

<213> Homo sapiens

<400> 465

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 gtggcaaatt agcaacaaat tctgacatca tatttatggg ttctgtatct ttgttgatga 120
 aggatggcac aatttttggc tgtgttcata atatactcag attagttcag ctccatcaga 180
 taaactggag acatgcagga cattagggta gtgttgtagc tctggtaatg a 231

<210> 466

<211> 231

<212> DNA

<213> Homo sapiens

<400> 466

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 cctgtgcaat caaatattgt ggagaattcc ctagctggag aagtcacaaa gactataggc 180
 aataatggag accagtccca caagatgaca accagtcgtt gtgtgcggct g 231

<210> 467

<211> 311

<212> DNA

<213> Homo sapiens

<400> 467

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 tgggtggcttt tctccttttt catcaagact cctcagcagg gagcccagac cagcctgcac 120
 tgtgccttaa cagaaggctc tgagattcta agtggaatc atttcagtga ctgtcatgtg 180
 gcatgggtct ctgcccagc tcgtaatgag actatagcaa ggcggctgtg ggacgtcagt 240
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 ctgcagcaga c 311

<210> 468

<211> 3112

<212> DNA

<213> Homo sapiens

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aagatctgca	tggtggaag	gacctgatga	tacagagttt	gataggagac	aattaaaggc	120
tggaaggcac	tggatgctg	atgatgaagt	ggactttcaa	actggggcac	tactgaaacg	180
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ccacagaggg	aatgtttatg	gggcacgttt	gtaagcctgg	gatgtgaagc	aaaggcaggg	2820
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<210> 469
 <211> 2229
 <212> DNA
 <213> Homo sapiens

<400> 469
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 <211> 2426
 <212> DNA
 <213> Homo sapiens

<400> 470
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caaaatttcta aagcgcactc accatgaaat ggataaaggt tacctttggg gatttgcaact 180
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 ccataaacat tccctctgtg gctcttgcac ttcatatatt tatctaaact cttataatca 360
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<212> DNA

<213> Homo sapiens

<400> 471

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<213> Homo sapiens

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<211> 1594

<212> DNA

<213> Homo sapiens

<400> 474

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<210> 476

<211> 3434

<212> DNA

<213> Homo sapiens

<400> 476

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 gccagtggta ccaccaggg gacttggtct tctgtggccc aggccagacg tagaatttga 240
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 gcagggccag gctggcttaa ggagcaagca gccacctctg ttaggggtgt gcctggagca 360
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 atccctttat ttttaagccta tgtgtgtctt tgcacatgag atgggtctcc tgaatacagg 660
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 ctaggatgaa gtatattgtt actgtgcttt gggattaaaa taagtaacta cagtttatag 2580
 aacttttata ctgatacaca gacactaaaa agggaaaggg tttagatgag aagctctgct 2640

<210> 477

<212> PRT

<213> Homo sapiens

<400> 477

Met Asp Gly His Thr Asp Ile Trp Arg Asn His Met Asp Thr Pro Pro
5 10 15

His Tyr His Arg Asp Thr Asp Thr Arg Arg His His His Met Asp Thr
20 25 30

Leu Ser His Tyr His Arg Asp Thr Arg His His Thr Val Thr Trp Thr
35 40 45

His His His Thr His Glu His Thr Asp Thr Leu Pro Tyr Gly His Trp
50 55 60

His Thr His Cys His Thr Val Thr Trp Thr His Leu His Thr Ile Thr
65 70 75 80

Pro Pro His Thr Leu Pro Val Asp Thr Arg Thr His Arg His Cys His
85 90 95

Thr Asp Thr Gln Asn Thr Val Thr Arg Arg His His His Ala Asp Thr
100 105 110

Pro Pro Leu Trp Cys Arg Leu Asn Tyr Pro Ala Gly Gly Thr Ala Val
115 120 125

Ala Tyr Ser Cys Leu Ser Asp Trp Leu Ser Pro Gln
130 135 140

<210> 478

<211> 143

<212> PRT

<213> Homo sapiens

<400> 478

Met Tyr Arg His Thr Glu Thr Leu Pro His Gly Asp Thr Val Thr Gln
 5 10 15

Ser His Gly His Thr Gly Ile Val Thr Trp Thr Asp Thr Gln Thr Tyr
 20 25 30

Gly Glu Ile Thr Trp Thr His His His Thr Ile Thr Gly Thr Gln Thr
 35 40 45

His Gly Asp Ile Thr Thr Trp Thr His Cys His Thr Thr Thr Gly Thr
 50 55 60

Arg Asp Ile Thr Leu Ser His Gly His Thr Ile Thr His Met Asn Thr
 65 70 75 80

Pro Thr His Cys His Met Asp Thr Gly Thr His Thr Ala Thr Leu Ser
 85 90 95

His Gly His Thr Ser Thr Pro Ser His His His Thr His Cys Leu Trp
 100 105 110

Thr Gln Gly His Thr Asp Thr Val Thr Gln Ile His Lys Thr Leu Ser
 115 120 125

His Gly Asp Ile Thr Met Gln Ile His His His Ser Gly Ala Val
 130 135 140

<210> 479

<211> 222

<212> PRT

<213> Homo sapiens

<400> 479

Met Tyr Arg His Thr Glu Thr Leu Pro His Gly Asp Thr Val Thr Gln
 5 10 15

Ser His Glu His Thr Gly Ile Val Thr Trp Thr Asp Thr Gln Thr Tyr
 20 25 30

Gly Glu Ile Thr Leu Thr His His His Thr Ile Thr Gly Thr Gln Thr
 35 40 45

His Gly Asp Ile Thr Thr Trp Thr His Cys His Thr Thr Thr Gly Thr
 50 55 60

Arg Asp Ile Thr Leu Ser His Gly His Thr Ile Thr His Met Asn Thr
 65 70 75 80

Pro Thr His Cys His Met Asp Thr Ala Thr His Thr Ala Thr Leu Ser
 85 90 95

His Gly His Thr Ser Ile Pro Ser His His His Thr His Cys His Val

006230 "SEAT9960"

100 105 110
 Asp Thr Arg Thr His Arg His Cys His Thr Asp Thr Gln Asn Thr Val
 115 120 125
 Thr Arg Arg His His His Ala Asp Thr Pro Pro His Gly His Ser Thr
 130 135 140
 Arg His Ser Ala Thr Gln Ile His His His Thr Glu Met Arg Thr His
 145 150 155 160
 Cys His Thr Asp Thr Thr Thr Ser Leu Pro His Phe His Val Ser Ala
 165 170 175
 Gly Gly Val Gly Pro Thr Thr Leu Gly Ser Asn Arg Glu Ile Thr Trp
 180 185 190
 Thr Tyr Ser Glu Gly Lys Ile Phe Phe Tyr Phe Leu Gly Asn Gln Ala
 195 200 205
 Arg Leu Cys Leu Lys Lys Arg Lys Lys Lys Gln Tyr Thr Val
 210 215 220

 <210> 480
 <211> 144
 <212> PRT
 <213> Homo sapiens

 <400> 480
 Met Glu Pro Tyr Arg Gly Asn Glu Gln Pro Ser Gln Glu Gln Gly Val
 5 10 15
 Cys Cys Leu Trp Gly Leu Gln Ser Leu Pro Gln Gly Ser Tyr Val Thr
 20 25 30
 Val Gly Phe Leu Val Val Lys Arg Gln Thr Ile Gly Arg Leu Glu Arg
 35 40 45
 Asp Phe Met Phe Lys Cys Arg Lys Gln Pro Gly Leu Pro Pro Ser Gly
 50 55 60
 Leu Cys Leu Leu Trp Pro Trp Pro Asn Leu Glu Phe Gly Arg Arg Gln
 65 70 75 80
 Asp Arg Leu Thr Trp Ser Ser Val Ser Val Ala Gly Val Cys Ala Cys
 85 90 95
 Arg Ala Arg Pro Gly Trp Leu Gly Glu Gln Pro Ala Thr Ser Ala Gly
 100 105 110
 Val Arg Leu Glu Gln Val Glu Gln Pro Pro Ala His Pro Leu Gln Glu
 115 120 125

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<210> 481
<211> 167
<212> PRT
<213> Homo sapiens
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Ala Leu Ala Ala Thr Ser Ala Gly Val Arg Leu Glu Gly Val Asp Arg
20 25 30

Leu Ser Gly Cys His Leu Met Ala Asp Gly Ala Lys Ala Leu Gly Lys
50 55 60

Cys Pro Ala Ala Ser Glu Val Gly Gly Cys Ala Pro Ser Ser Trp Arg
85 90 95

Gln His Ala Gln Ala Ser Val Leu Leu Leu Cys Tyr Lys Trp Ser His
115 120 125

Gly Gly Ser Ser Pro Cys Leu Lys Gly Leu Met Ser Leu Trp Ala Ser
145 150 155 160

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<210> 482
<211> 143
<212> PRT
<213> Homo sapiens
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<400> 482
Met Glu Pro Tyr Arg Gly Asn Lys Lys Gln Val Gln Glu Lys Gly Val

5 10 15
 Pro Cys Leu Trp Gly Ser Ser Pro Cys Leu Arg Cys His Met Ala Leu
 20 25 30
 Arg Ala Ser Trp Leu Pro Gly Gly Gly Pro Gln Ala Ile Leu Gly Arg
 35 40 45
 Thr Leu Cys Ser Ser Ala Glu Ser Ser Gln Asp Cys His Pro Gly Gly
 50 55 60
 Pro Ser Ile Ala Leu Ala Lys Pro Cys Arg Gly Val Trp Leu Leu Phe
 65 70 75 80
 Glu Pro Ala Trp Pro Pro Trp His Ala Arg Ala Pro Gly Ala Gly Thr
 85 90 95
 Leu Leu Arg Val Cys Leu Ser Cys Leu Gly Cys His Leu Cys Gly Gly
 100 105 110
 Ala Ser Gly Gly Gly Gly Pro Ala Thr Asn Leu Thr Gln Ser Arg Lys
 115 120 125
 Trp Met Ala Met Phe Pro Gln Pro Glu Trp Leu Pro Pro Asp Gly
 130 135 140

 <210> 483
 <211> 143
 <212> PRT
 <213> Homo sapiens

 <400> 483
 Met Glu Thr Gln Arg Gly Asn Lys Gln Arg Ala Gln Glu Gln Gly Val
 5 10 15
 Cys Cys Leu Trp Gly Ser Ser Pro Cys Leu Gly Ser Tyr Gly Thr Ala
 20 25 30
 Gly Phe Leu Val Ala Lys Arg Arg Thr Thr Gly Leu Leu Glu Glu Asp
 35 40 45
 Phe Thr Phe Lys Cys Arg Lys Gln Pro Lys Leu Pro Ser Met Arg Leu
 50 55 60
 Ser Leu Leu Trp Pro Trp Arg Asp Leu Lys Phe Val Pro Arg Gln Asp
 65 70 75 80
 Lys Leu Thr Arg Ser Ser Val Ser Val Ala Gly Ala Tyr Ala Cys Arg
 85 90 95
 Ala Gly Pro Gly Trp Leu Lys Glu Gln Pro Ala Thr Ser Ala Arg Val
 100 105 110

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<210> 488
<211> 33
<212> DNA
<213> Artificial Sequence
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<220>
<223> Made in a lab

<400> 488
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33

<210> 489
<211> 19
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 489
Met Asp Arg Leu Val Gln Arg Phe Gly Thr Arg Ala Val Tyr Leu Ala
1 5 10 15
Ser Val Ala

<210> 490
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 490
Tyr Leu Ala Ser Val Ala Ala Phe Pro Val Ala Ala Gly Ala Thr Cys
1 5 10 15
Leu Ser His Ser
20

<210> 491
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 491
Thr Cys Leu Ser His Ser Val Ala Val Val Thr Ala Ser Ala Ala Leu
1 5 10 15
Thr Gly Phe Thr
20

<210> 492
<211> 20
<212> PRT
<213> Artificial Sequence

006330 "GTCGTGCG"

<220>

<223> Made in a lab

<400> 492

Ala	Leu	Thr	Gly	Phe	Thr	Phe	Ser	Ala	Leu	Gln	Ile	Leu	Pro	Tyr	Thr
1				5					10					15	
Leu	Ala	Ser	Leu												
				20											

<210> 493

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 493

Tyr	Thr	Leu	Ala	Ser	Leu	Tyr	His	Arg	Glu	Lys	Gln	Val	Phe	Leu	Pro
1				5					10					15	
Lys	Tyr	Arg	Gly												
				20											

<210> 494

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 494

Leu	Pro	Lys	Tyr	Arg	Gly	Asp	Thr	Gly	Gly	Ala	Ser	Ser	Glu	Asp	Ser
1				5				10						15	
Leu	Met	Ile	Ser												
				20											

<210> 495

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 495

Asp	Ser	Leu	Met	Thr	Ser	Phe	Leu	Pro	Gly	Pro	Lys	Pro	Gly	Ala	Pro
1				5					10					15	
Phe	Pro	Asn	Gly												
				20											

<210> 496

<211> 21

006630 " 3e at 6950

<212> PRT
 <213> Artificial Sequence

<220>
 <223> Made in a lab

<400> 496
 Ala Pro Phe Pro Asn Gly His Val Gly Ala Gly Gly Ser Gly Leu Leu
 1 5 10 15
 Pro Pro Pro Pro Ala
 20

<210> 497
 <211> 20
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Made in a lab

<400> 497
 Leu Leu Pro Pro Pro Ala Leu Cys Gly Ala Ser Ala Cys Asp Val
 1 5 10 15
 Ser Val Arg Val
 20

<210> 498
 <211> 20
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Made in a lab

<400> 498
 Asp Val Ser Val Arg Val Val Val Gly Glu Pro Thr Glu Ala Arg Val
 1 5 10 15
 Val Pro Gly Arg
 20

<210> 499
 <211> 20
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Made in a lab

<400> 499
 Arg Val Val Pro Gly Arg Gly Ile Cys Leu Asp Leu Ala Ile Leu Asp
 1 5 10 15
 Ser Ala Phe Leu
 20

006360"SEC2350

<210> 500
 <211> 20
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Made in a lab

<400> 500
 Leu Asp Ser Ala Phe Leu Leu Ser Gln Val Ala Pro Ser Leu Phe Met
 1 5 10 15
 Gly Ser Ile Val
 20

<210> 501
 <211> 20
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Made in a lab

<400> 501
 Phe Met Gly Ser Ile Val Gln Leu Ser Gln Ser Val Thr Ala Tyr Met
 1 5 10 15
 Val Ser Ala Ala
 20

<210> 502
 <211> 414
 <212> DNA
 <213> Homo Sapien

<220>
 <221> misc_feature
 <222> (1)...(414)
 <223> n=A,T,C or G

<400> 502
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 tcagtcggtg gaggagtccg ggggtcgct ggtcacgctt gggacacctt tgacantcac 120
 ctgtagagtt tttggaatng acctcagtag caatgcaatg agctgggtcc gccaggctcc 180
 agggaagggg ctggaatgga tcggagccat tgataattgt ccacantacg cgacctgggc 240
 gaaaggccga ttnatnatntt ccaaaacctn gaccacggtg gatttgaaaa tgaccagtcc 300
 gacaaccgag gacacggcca cctatttttg tggcagaatg aatactggta atagtgggtg 360
 gaagaatatt tggggcccag gcaccctggt caccgtntcc tcagggcaac ctaa 414

<210> 503
 <211> 379
 <212> DNA
 <213> Homo Sapien

<220>
 <221> misc_feature

<222> (1)...(379)

<223> n=A,T,C or G

<400> 503

atnccgatggt	gcttgggtcaa	aggtgtccag	tgctcagtcgg	tggaggagtc	cggggggtcgc	60
ctggtcacgc	ctgggacacc	cctgacactc	acctgcaccg	tntctggatt	ngacatcagt	120
agctatggag	tgagctgggt	ccgccaggct	ccagggaagg	ggctgggnata	catcggtatca	180
ttagtagtag	tggtacattt	tacgcgagct	gggcgaaagg	ccgattcacc	atttcacaaa	240
cctngaccac	ggtggatttg	aaaatcacca	gtttgacaac	cgaggacacg	gccacctatt	300
tntgtgccag	aggggggttt	aattataaag	acatttgggg	cccaggcacc	ctggtcaccg	360
tntccttagg	gcaacctaa					379

<210> 504

<211> 19

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 504

Gly	Phe	Thr	Asn	Tyr	Thr	Asp	Phe	Glu	Asp	Ser	Pro	Tyr	Phe	Lys	Glu
1				5				10						15	
Asn	Ser	Ala													

<210> 505

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 505

Lys	Glu	Asn	Ser	Ala	Phe	Pro	Pro	Phe	Cys	Cys	Asn	Asp	Asn	Val	Thr
1				5				10						15	
Asn	Thr	Ala	Asn												
				20											

<210> 506

<211> 407

<212> DNA

<213> Homo Sapien

<400> 506

atggagacag	gcctgcgctg	gcttctcctg	gtcgtcgcgc	tcaaagggtg	ccagtgtcag	60
tcgctggagg	agtcggggg	tcgcctggtc	acgcctggga	cacctctgac	actcacctgc	120
accgtctctg	gattctccct	cagtagcaat	gcaatgatct	gggtccgcc	ggctccagg	180
aaggggctgg	aatacatcgg	atacattagt	tatgggtgga	gcgcatacta	cgcgagctgg	240
gtgaaaggcc	gattcaccat	ctccaaaacc	tgcaccacgg	tggatctgag	aatgaccagt	300
ctgacaaccg	aggacacggc	cacctatttc	tgtgccagaa	atagtgattt	tagtggtatg	360
ttgtggggcc	caggcaccct	ggtcaccgtc	tcctcagggc	aacctaa		407

006230" 9E2F5960

<210> 507
 <211> 422
 <212> DNA
 <213> Homo Sapien

<400> 507
 atggagacag gcctgcgctg gcttctcctg gtcgctgtgc tcaaaggtgt ccagtgtcag 60
 tcggtggagg agtccggggg tcgcctgggc acgcctggga caccctgac actcacctgt 120
 acagtctctg gattctccct cagcaactac gacctgaact gggcccgcca ggctccaggg 180
 aaggggctgg aatggatcgg gatcattaat tatgttggtg ggacggacta cgcgaactgg 240
 gcaaaaggcc gggttcacat ctccaaaacc tcgaccaccg tggatctcaa gatcgccagt 300
 ccgacaaccg aggacacggc cacctatttc tgtgccagag ggtggaagtg cgatgagtct 360
 ggtccgtgct tgcgcatctg gggcccaggc accctgggtc ccgtctcctt agggcaacct 420
 aa 422

<210> 508
 <211> 411
 <212> DNA
 <213> Homo Sapien

<220>
 <221> misc_feature
 <222> (1)...(411)
 <223> n=A,T,C or G

<400> 508
 atggagacag gcctcgctgg cttctcctgg tcgctgtgct caaaggtgtc cagtgtcagt 60
 cgggtggagg gtccgggggt cgctcggtca cgctggggac accctgaca ctcacctgca 120
 cagtctctgg aatcgacctc agtagctact gcatgagctg ggtccgccag gctccaggga 180
 aggggctgga atggatcgga atcattggta ctctcggtga cacatactac gcgaggtggg 240
 cgaaaggccg attcaccatc tccaaaacct cgaccacggg gcatntgaaa atcnccagtc 300
 cgacaaccga ggacacggcc acctatttct gtgccagaga tcttcgggat ggtagtagta 360
 ctgggttatta taaaatctgg ggcccaggca ccttggtcac cgtctccttg g 411

<210> 509
 <211> 15
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Made in a lab

<400> 509
 Leu Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser
 1 5 10 15

<210> 510
 <211> 15
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Made in a lab

<400> 510
 Pro Glu Tyr Asn Arg Pro Leu Leu Ala Asn Asp Leu Met Leu Ile
 1 5 10 15

<210> 511
 <211> 15
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Made in a lab

<400> 511

Tyr His Pro Ser Met Phe Cys Ala Gly Gly Gly Gln Asp Gln Lys
 1 5 10 15

<210> 512
 <211> 15
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Made in a lab

<400> 512
 Asp Ser Gly Gly Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu
 1 5 10 15

<210> 513
 <211> 15
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Made in a lab

<400> 513
 Ala Pro Cys Gly Gln Val Gly Val Pro Asx Val Tyr Thr Asn Leu
 1 5 10 15

<210> 514
 <211> 15
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Made in a lab

<400> 514
 Leu Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser
 1 5 10 15

006330 "SECRET" 006330

<220>
<223> Made in a lab

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<210> 516
<211> 15
<212> PRT
<213> Artificial Sequence
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<220>
<223> Made in a lab

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<210> 517
<211> 15
<212> PRT
<213> Artificial Sequence
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<220>
<223> Made in a lab

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<210> 518
<211> 15
<212> PRT
<213> Artificial Sequence
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<220>
<223> Made in a lab

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<210> 519
<211> 17
<212> PRT
<213> Artificial Sequence
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<223> Made in a lab

<400> 519

Arg Ala Glu Pro Gly Thr Glu Ala Arg Arg Asn Tyr Asp Glu Gly Cys
 1 5 10 15
 Gly

<210> 520

<211> 25

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 520

Val Gly Glu Gly Leu Tyr Gln Gly Val Pro Arg Ala Glu Pro Gly Thr
 1 5 10 15
 Glu Ala Arg Arg His Tyr Asp Glu Gly
 20 25

<210> 521

<211> 21

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 521

Ala Pro Phe Pro Asn Gly His Val Gly Ala Gly Gly Ser Gly Leu Leu
 1 5 10 15
 Pro Pro Pro Pro Ala
 20

<210> 522

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 522

Leu Leu Val Val Pro Ala Ile Lys Lys Asp Tyr Gly Ser Gln Glu Asp
 1 5 10 15
 Phe Thr Gln Val
 20

<210> 523

<211> 254

<212> PRT

<213> Artificial Sequence

006230" SEAT 5960

<223> Made in a lab

<221> VARIANT

<223> Xaa = any amino acid

Met 1	Ala	Thr	Ala	Gly 5	Asn	Pro	Trp	Gly	Trp 10	Phe	Leu	Gly	Tyr	Leu 15	Ile
Leu	Gly	Val	Ala 20	Gly	Ser	Leu	Val	Ser 25	Gly	Ser	Cys	Ser	Gln 30	Ile	Ile
Asn	Gly	Glu	Asp 35	Cys	Ser	Pro	His 40	Ser	Gln	Pro	Trp	Gln 45	Ala	Ala	Leu
Val	Met 50	Glu	Asn	Glu	Leu	Phe 55	Cys	Ser	Gly	Val	Leu 60	Val	His	Pro	Gln
Trp 65	Val	Leu	Ser	Ala 70	Thr	His	Cys	Phe	Gln 75	Asn	Ser	Tyr	Thr	Ile	Gly 80
Leu	Gly	Leu	His 85	Ser	Leu	Glu	Ala	Asp 90	Gln	Glu	Pro	Gly	Ser	Gln 95	Met
Val	Glu	Ala	Ser 100	Leu	Ser	Val	Arg 105	His	Pro	Glu	Tyr	Asn 110	Arg	Pro	Leu
Leu	Ala	Asn 115	Asp	Leu	Met	Leu	Ile 120	Lys	Leu	Asp	Glu 125	Ser	Val	Ser	Glu
Ser	Asp 130	Thr	Ile	Arg	Ser	Ile 135	Ser	Ile	Ala	Ser	Gln 140	Cys	Pro	Thr	Ala
Gly 145	Asn	Ser	Cys 150	Leu	Val	Ser	Gly	Trp	Gly	Leu 155	Leu	Ala	Asn	Gly 160	Arg
Met	Pro	Thr	Val 165	Leu	Gln	Cys	Val	Asn	Val 170	Ser	Val	Val	Ser	Glu 175	Glu
Val	Cys	Ser	Lys 180	Leu	Tyr	Asp	Pro	Leu 185	Tyr	His	Pro	Ser	Met 190	Phe	Cys
Ala	Gly	Gly	Gly 195	Gln	Xaa	Gln	Xaa 200	Asp	Ser	Cys	Asn 205	Gly	Asp	Ser	Gly
Gly	Pro 210	Leu	Ile	Cys	Asn	Gly 215	Tyr	Leu	Gln	Gly	Leu 220	Val	Ser	Phe	Gly
Lys 225	Ala	Pro	Cys 230	Gly	Gln	Val	Gly	Val	Pro	Gly 235	Val	Tyr	Thr	Asn 240	Leu
Cys	Lys	Phe	Thr 245	Glu	Trp	Ile	Glu	Lys 250	Thr	Val	Gln	Ala	Ser		

<213> Homo sapien

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tgcagaccct	ggcaggcggc	actggtcatg	gaaaacgaat	tgttctccta	gggcgtcctg	180
gtgcatccgc	agtgggtgct	gtcagccgca	cactgtttcc	agaactcctc	caccatcggg	240
ctgggacctgc	acagtcttga	ggccgaccaa	gagccaggga	gcagatgggt	ggaggccagc	300

```

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gactcctgca acggtgactc tggggggccc ctgatctgca acgggtactt gcagggcctt 660
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<210> 525

<211> 254

<212> PRT

<213> Homo sapien

<400> 525

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Leu Gly Val Ala Gly Ser Leu Val Ser Gly Ser Cys Ser Gln Ile Ile
          20          25          30
Asn Gly Glu Asp Cys Ser Pro His Ser Gln Pro Trp Gln Ala Ala Leu
          35          40          45
Val Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln
          50          55          60
Trp Val Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly
          65          70          75          80
Leu Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met
          85          90          95
Val Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu
          100          105          110
Leu Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu
          115          120          125
Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala
          130          135          140
Gly Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg
          145          150          155          160
Met Pro Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu Glu
          165          170          175
Val Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys
          180          185          190
Ala Gly Gly Gly Gln Asp Gln Lys Asp Ser Cys Asn Gly Asp Ser Gly
          195          200          205
Gly Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly
          210          215          220
Lys Ala Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn Leu
          225          230          235          240
Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser
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<210> 526

<211> 963

<212> DNA

<213> Homo sapiens

<400> 526


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aactgcatcg tgggtcttcat cgtaaggacg gaacgcagcc tgcacgctcc gatgtacctc 180
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```

<210> 527

<211> 320

<212> PRT

<213> Homo sapiens

<400> 527

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Met Ser Ser Cys Asn Phe Thr His Ala Thr Phe Val Leu Ile Gly Ile
      5                      10                      15

```

```

Pro Gly Leu Glu Lys Ala His Phe Trp Val Gly Phe Pro Leu Leu Ser
      20                      25                      30

```

```

Met Tyr Val Val Ala Met Phe Gly Asn Cys Ile Val Val Phe Ile Val
      35                      40                      45

```

```

Arg Thr Glu Arg Ser Leu His Ala Pro Met Tyr Leu Phe Leu Cys Met
      50                      55                      60

```

```

Leu Ala Ala Ile Asp Leu Ala Leu Ser Thr Ser Thr Met Pro Lys Ile
      65                      70                      75                      80

```

```

Leu Ala Leu Phe Trp Phe Asp Ser Arg Glu Ile Ser Phe Glu Ala Cys
      85                      90                      95

```

```

Leu Thr Gln Met Phe Phe Ile His Ala Leu Ser Ala Ile Glu Ser Thr
      100                     105                     110

```

```

Ile Leu Leu Ala Met Ala Phe Asp Arg Tyr Val Ala Ile Cys His Pro
      115                     120                     125

```

```

Leu Arg His Ala Ala Val Leu Asn Asn Thr Val Thr Ala Gln Ile Gly
      130                     135                     140

```

```

Ile Val Ala Val Val Arg Gly Ser Leu Phe Phe Phe Pro Leu Pro Leu
      145                     150                     155                     160

```

006230 " G E A T S G S O

Leu Ile Lys Arg Leu Ala Phe Cys His Ser Asn Val Leu Ser His Ser
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 Tyr Cys Val His Gln Asp Val Met Lys Leu Ala Tyr Ala Asp Thr Leu
 180 185 190
 Pro Asn Val Val Tyr Gly Leu Thr Ala Ile Leu Leu Val Met Gly Val
 195 200 205
 Asp Val Met Phe Ile Ser Leu Ser Tyr Phe Leu Ile Ile Arg Thr Val
 210 215 220
 Leu Gln Leu Pro Ser Lys Ser Glu Arg Ala Lys Ala Phe Gly Thr Cys
 225 230 235 240
 Val Ser His Ile Gly Val Val Leu Ala Phe Tyr Val Pro Leu Ile Gly
 245 250 255
 Leu Ser Val Val His Arg Phe Gly Asn Ser Leu His Pro Ile Val Arg
 260 265 270
 Val Val Met Gly Asp Ile Tyr Leu Leu Leu Pro Pro Val Ile Asn Pro
 275 280 285
 Ile Ile Tyr Gly Ala Lys Thr Lys Gln Ile Arg Thr Arg Val Leu Ala
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<210> 528
 <211> 20
 <212> DNA
 <213> Homo Sapien

<400> 528
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<210> 529
 <211> 20
 <212> DNA
 <213> Homo Sapien

<400> 529
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<210> 530
 <211> 1852
 <212> DNA
 <213> Homo sapiens

<400> 530
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<210> 531

<211> 879

<212> DNA

<213> Homo sapiens

<400> 531

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tgcaagtggg gctgccactg cttccccctg tgcaggggga gcggaagag caacgtgggtc 180
gcttggggag actacgatga cagcgcttcc atggatccca ggtaccacgt ccatggagaa 240
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cttaatgtcc ttgacaacaa aaagaggaca gctctgacaa aggcctgaca atgccaggaa 480
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<210> 532

<211> 292

<212> PRT

<213> Homo sapiens

<400> 532

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Met His Leu Ser Phe Pro Ala Phe Leu Pro Pro Trp Met Asp Arg Gly
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Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp His Asn Asp Ser Ser
              20              25              30

Val Lys Thr Leu Gly Ser Lys Arg Cys Lys Trp Cys Cys His Cys Phe
              35              40              45

Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val Val Ala Trp Gly Asp
              50              55              60

Tyr Asp Asp Ser Ala Phe Met Asp Pro Arg Tyr His Val His Gly Glu
              65              70              75              80

Asp Leu Asp Lys Leu His Arg Ala Ala Trp Trp Gly Lys Val Pro Arg
              85              90              95

Lys Asp Leu Ile Val Met Leu Arg Asp Thr Asp Val Asn Lys Arg Asp
              100              105              110

Lys Gln Lys Arg Thr Ala Leu His Leu Ala Ser Ala Asn Gly Asn Ser
              115              120              125

Glu Val Val Lys Leu Val Leu Asp Arg Arg Cys Gln Leu Asn Val Leu
              130              135              140

Asp Asn Lys Lys Arg Thr Ala Leu Thr Lys Ala Val Gln Cys Gln Glu
              145              150              155              160

Asp Glu Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro Asn Ile
              165              170              175

Pro Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr Ala Val Tyr Asn Glu
              180              185              190

Asp Lys Leu Met Ala Lys Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu
              195              200              205

Ser Lys Asn Lys His Gly Leu Thr Pro Leu Leu Leu Gly Ile His Glu
              210              215              220

Gln Lys Gln Gln Val Val Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu
              225              230              235              240

Asn Ala Leu Asp Arg Tyr Gly Arg Thr Ala Leu Ile Leu Ala Val Cys
              245              250              255

Cys Gly Ser Ala Ser Ile Val Ser Pro Leu Leu Glu Gln Asn Val Asp
              260              265              270

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006630 "SEAT5960"

Val Ser Ser Gln Asp Leu Glu Arg Arg Pro Glu Ser Met Leu Phe Leu
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Val Ile Ile Met
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<210> 533
 <211> 801
 <212> DNA
 <213> Homo sapiens

<400> 533
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<210> 534
 <211> 266
 <212> PRT
 <213> Homo sapiens

<400> 534
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 Arg Lys Gln Ala Ala Gly Ser Gly Ala Gly Tyr Ala Leu Pro Ser Ala
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 Leu Gln Ser Met Pro Gln Gly Ser Tyr Ala Thr Ala Arg Phe Leu Val
 35 40 45
 Ala Lys Arg Pro Thr Thr Gly His Leu Glu Lys Glu Phe Met Phe His
 50 55 60
 Cys Arg Lys Gln Pro Gly Ser Pro Ser Arg Gly Leu Gly Leu Leu Trp
 65 70 75 80
 Pro Trp Pro Asp Ile Glu Phe Val Pro Arg Gln Asp Lys Leu Thr Gln
 85 90 95
 Ser Ser Val Leu Val Pro Gln Ile Cys Ala Cys Gln Thr Arg Pro Asn

005330 "GCTGCA" 533

100 105 110
 Trp Leu Asn Glu Gln Pro Ala Thr Ser Ala Gly Val Arg Leu Glu Glu
 115 120 125
 Val Asp Gln Pro Pro Thr Leu Pro Ser Gln Gly Ser Gly Trp Pro Cys
 130 135 140
 Ser His Ser Leu Ser Gly Cys His Leu Met Ala Asp Ile Ala Lys Ala
 145 150 155 160
 Leu Gly Lys Ala Asp Gly Pro Trp Pro Tyr Leu Phe Val Arg Arg Thr
 165 170 175
 Asp Val Pro Cys Pro Ala Ala Ser Glu Val Gly Gly Cys Ala Pro Ser
 180 185 190
 Ser Trp His Thr Leu Ala Glu Val Thr Gly Cys Ser Leu Ser Pro Leu
 195 200 205
 Ser Leu Ala Gln His Ala Gln Ala Ser Val Leu Leu Leu Cys Tyr Lys
 210 215 220
 Trp Ser His Ile Gly Glu Thr Ser Ser His Leu Arg Ser Lys Val Tyr
 225 230 235 240
 Ala Ala Phe Gly Gly Ser Ser Pro Cys Leu Lys Gly Leu Met Ser Leu
 245 250 255
 Trp Ala Ser Trp Leu Pro Arg Gly Arg Pro
 260 265

<210> 535

<211> 6082

<212> DNA

<213> Homo sapiens

<400> 535

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<213> Homo sapiens

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25

30

Ile Gly His Lys Arg Arg Leu Glu Glu Asp Asp Met Tyr Ser Val Leu

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Cys	Ala	Gly	Met	Arg	Leu	Arg	Val	Ala	Met	Cys	His	Met	Ile	Tyr	Arg
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Lys	Ala	Leu	Arg	Leu	Ser	Asn	Met	Ala	Met	Gly	Lys	Thr	Thr	Thr	Gly
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Gln	Ile	Val	Asn	Leu	Leu	Ser	Asn	Asp	Val	Asn	Lys	Phe	Asp	Gln	Val
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Ala Ile Pro Leu Val Pro Leu Gly Ile Ile Phe Ile Phe Leu Arg Arg															
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 Tyr Leu Val Leu Gly Ile Phe Thr Leu Ile Glu Glu Ser Ala Lys Val
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 Phe Tyr His Val Gln Cys Ala Gly Met Arg Leu Arg Val Ala Met Cys
 115 120 125

 His Met Ile Tyr Arg Lys Ala Leu Arg Leu Ser Asn Met Ala Met Gly
 130 135 140

 Lys Thr Thr Thr Gly Gln Ile Val Asn Leu Leu Ser Asn Asp Val Asn
 145 150 155 160

 Lys Phe Asp Gln Val Thr Val Phe Leu His Phe Leu Trp Ala Gly Pro
 165 170 175

 Leu Gln Ala Ile Ala Val Thr Ala Leu Leu Trp Met Glu Ile Gly Ile
 180 185 190

 Ser Cys Leu Ala Gly Met Ala Val Leu Ile Ile Leu Leu Pro Leu Gln
 195 200 205

 Ser Cys Phe Gly Lys Leu Phe Ser Ser Leu Arg Ser Lys Thr Ala Thr

006230" 922T5960

210					215					220					
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Arg	Ile	Ile	Lys	Met 245	Tyr	Ala	Trp	Glu	Lys 250	Ser	Phe	Ser	Asn	Leu	Ile 255
Thr	Asn	Leu	Arg 260	Lys	Lys	Glu	Ile	Ser 265	Lys	Ile	Leu	Arg	Ser 270	Ser	Cys
Leu	Arg	Gly 275	Met	Asn	Leu	Ala	Ser 280	Phe	Phe	Ser	Ala	Ser 285	Lys	Ile	Ile
Val	Phe 290	Val	Thr	Phe	Thr	Thr 295	Tyr	Val	Leu	Leu	Gly 300	Ser	Val	Ile	Thr
Ala 305	Ser	Arg	Val	Phe	Val 310	Ala	Val	Thr	Leu	Tyr 315	Gly	Ala	Val	Arg	Leu 320
Thr	Val	Thr	Leu	Phe 325	Phe	Pro	Ser	Ala	Ile 330	Glu	Arg	Val	Ser	Glu	Ala 335
Ile	Val	Ser	Ile 340	Arg	Arg	Ile	Gln	Thr 345	Phe	Leu	Leu	Leu	Asp 350	Glu	Ile
Ser	Gln	Arg 355	Asn	Arg	Gln	Leu	Pro 360	Ser	Asp	Gly	Lys	Lys 365	Met	Val	His
Val 370	Gln	Asp	Phe	Thr	Ala	Phe 375	Trp	Asp	Lys	Ala	Ser 380	Glu	Thr	Pro	Thr
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Gly	Glu	Leu	Ala 420	Pro	Ser	His	Gly	Leu 425	Val	Ser	Val	His	Gly 430	Arg	Ile
Ala	Tyr	Val 435	Ser	Gln	Gln	Pro	Trp 440	Val	Phe	Ser	Gly	Thr 445	Leu	Arg	Ser
Asn 450	Ile	Leu	Phe	Gly	Lys	Lys 455	Tyr	Glu	Lys	Glu	Arg 460	Tyr	Glu	Lys	Val
Ile 465	Lys	Ala	Cys	Ala	Leu	Lys	Lys	Asp	Leu	Gln 475	Leu	Leu	Glu	Asp	Gly 480
Asp	Leu	Thr	Val	Ile 485	Gly	Asp	Arg	Gly	Thr 490	Thr	Leu	Ser	Gly	Gly	Gln 495
Lys	Ala	Arg	Val	Asn	Leu	Ala	Arg	Ala	Val	Tyr	Gln	Asp	Ala	Asp	Ile

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Tyr	Leu	Leu	Asp	Asp	Pro	Leu	Ser	Ala	Val	Asp	Ala	Glu	Val	Ser	Arg
	515						520					525			
His	Leu	Phe	Glu	Leu	Cys	Ile	Cys	Gln	Ile	Leu	His	Glu	Lys	Ile	Thr
	530					535					540				
Ile	Leu	Val	Thr	His	Gln	Leu	Gln	Tyr	Leu	Lys	Ala	Ala	Ser	Gln	Ile
545					550					555					560
Leu	Ile	Leu	Lys	Asp	Gly	Lys	Met	Val	Gln	Lys	Gly	Thr	Tyr	Thr	Glu
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Phe	Leu	Lys	Ser	Gly	Ile	Asp	Phe	Gly	Ser	Leu	Leu	Lys	Lys	Asp	Asn
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Glu	Glu	Ser	Glu	Gln	Pro	Pro	Val	Pro	Gly	Thr	Pro	Thr	Leu	Arg	Asn
		595					600					605			
Arg	Thr	Phe	Ser	Glu	Ser	Ser	Val	Trp	Ser	Gln	Gln	Ser	Ser	Arg	Pro
	610						615								
Ser	Leu	Lys	Asp	Gly	Ala	Leu	Glu	Ser	Gln	Asp	Thr	Glu	Asn	Val	Pro
625					630					635					640
Val	Thr	Leu	Ser	Glu	Glu	Asn	Arg	Ser	Glu	Gly	Lys	Val	Gly	Phe	Gln
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Ala	Tyr	Lys	Asn	Tyr	Phe	Arg	Ala	Gly	Ala	His	Trp	Ile	Val	Phe	Ile
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Phe	Leu	Ile	Leu	Leu	Asn	Thr	Ala	Ala	Gln	Val	Ala	Tyr	Val	Leu	Gln
		675					680					685			
Asp	Trp	Trp	Leu	Ser	Tyr	Trp	Ala	Asn	Lys	Gln	Ser	Met	Leu	Asn	Val
	690					695					700				
Thr	Val	Asn	Gly	Gly	Gly	Asn	Val	Thr	Glu	Lys	Leu	Asp	Leu	Asn	Trp
705					710					715					720
Tyr	Leu	Gly	Ile	Tyr	Ser	Gly	Leu	Thr	Val	Ala	Thr	Val	Leu	Phe	Gly
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Thr	Leu	His	Asn	Lys	Met	Phe	Glu	Ser	Ile	Leu	Lys	Ala	Pro	Val	Leu
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006230" SEAT 5960

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 Ile Gln Thr Leu Leu Gln Val Val Gly Val Val Ser Val Ala Val Ala
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 Val Ile Pro Trp Ile Ala Ile Pro Leu Val Pro Leu Gly Ile Ile Phe
 820 825 830
 Ile Phe Leu Arg Arg Tyr Phe Leu Glu Thr Ser Arg Asp Val Lys Arg
 835 840 845
 Leu Glu Ser Thr Thr Arg Ser Pro Val Phe Ser His Leu Ser Ser Ser
 850 855 860
 Leu Gln Gly Leu Trp Thr Ile Arg Ala Tyr Lys Ala Glu Glu Arg Cys
 865 870 875 880
 Gln Glu Leu Phe Asp Ala His Gln Asp Leu His Ser Glu Ala Trp Phe
 885 890 895
 Leu Phe Leu Thr Thr Ser Arg Trp Phe Ala Val Arg Leu Asp Ala Ile
 900 905 910
 Cys Ala Met Phe Val Ile Ile Val Ala Phe Gly Ser Leu Ile Leu Ala
 915 920 925
 Lys Thr Leu Asp Ala Gly Gln Val Gly Leu Ala Leu Ser Tyr Ala Leu
 930 935 940
 Thr Leu Met Gly Met Phe Gln Trp Cys Val Arg Gln Ser Ala Glu Val
 945 950 955 960
 Glu Asn Met Met Ile Ser Val Glu Arg Val Ile Glu Tyr Thr Asp Leu
 965 970 975
 Glu Lys Glu Ala Pro Trp Glu Tyr Gln Lys Arg Pro Pro Pro Ala Trp
 980 985 990
 Pro His Glu Gly Val Ile Ile Phe Asp Asn Val Asn Phe Met Tyr Ser
 995 1000 1005
 Pro Gly Gly Pro Leu Val Leu Lys His Leu Thr Ala Leu Ile Lys Ser
 1010 1015 1020
 Gln Glu Lys Val Gly Ile Val Gly Arg Thr Gly Ala Gly Lys Ser Ser
 1025 1030 1035 1040
 Leu Ile Ser Ala Leu Phe Arg Leu Ser Glu Pro Glu Gly Lys Ile Trp
 1045 1050 1055
 Ile Asp Lys Ile Leu Thr Thr Glu Ile Gly Leu His Asp Leu Arg Lys
 1060 1065 1070
 Lys Met Ser Ile Ile Pro Gln Glu Pro Val Leu Phe Thr Gly Thr Met

006230-925960

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Arg Lys Asn Leu Asp Pro Phe Asn Glu His Thr Asp Glu Glu Leu Trp		
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Asn Ala Leu Gln Glu Val Gln Leu Lys Glu Thr Ile Glu Asp Leu Pro		
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Gly Lys Met Asp Thr Glu Leu Ala Glu Ser Gly Ser Asn Phe Ser Val		
	1125	1130 1135
Gly Gln Arg Gln Leu Val Cys Leu Ala Arg Ala Ile Leu Arg Lys Asn		
	1140	1145 1150
Gln Ile Leu Ile Ile Asp Glu Ala Thr Ala Asn Val Asp Pro Arg Thr		
	1155	1160 1165
Asp Glu Leu Ile Gln Lys Lys Ile Arg Glu Lys Phe Ala His Cys Thr		
	1170	1175 1180
Val Leu Thr Ile Ala His Arg Leu Asn Thr Ile Ile Asp Ser Asp Lys		
	1185	1190 1195 1200
Ile Met Val Leu Asp Ser Gly Arg Leu Lys Glu Tyr Asp Glu Pro Tyr		
	1205	1210 1215
Val Leu Leu Gln Asn Lys Glu Ser Leu Phe Tyr Lys Met Val Gln Gln		
	1220	1225 1230
Leu Gly Lys Ala Glu Ala Ala Ala Leu Thr Glu Thr Ala Lys Gln Arg		
	1235	1240 1245
Trp Gly Phe Thr Met Leu Ala Arg Leu Val Ser Asn Ser		
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<213> Artificial Sequence

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<223> Made in a lab

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<212> PRT

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006630" 3275960

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Ser Val

<210> 546
 <211> 29
 <212> PRT
 <213> Homo sapiens

<400> 546
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Thr Glu Ala Arg Arg His Tyr Asp Glu Gly Val Arg Met
 20 25

<210> 547
 <211> 58
 <212> PRT
 <213> Homo sapiens

<400> 547
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 20 25 30

Ala Phe Arg Asn Leu Gly Ala Leu Leu Pro Arg Leu His Gln Leu Cys
 35 40 45

Cys Arg Met Pro Arg Thr Leu Arg Arg Leu
 50 55

<210> 548
 <211> 18
 <212> PRT
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Glu Cys

<210> 549
 <211> 18

006230" SEAT590

<212> PRT
 <213> Homo sapiens

<400> 549
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Gln Ala

<210> 550
 <211> 14
 <212> PRT
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<400> 550
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 <212> DNA
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 tcataccagt ccacggacta ttatgaacca caccacacag gaggaggtga gcactaggca 180
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<210> 553

<211> 58

<212> PRT

<213> Homo sapiens

<400> 553

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Phe Leu Thr Phe Ser Phe Leu Ser Met Val Glu Pro Pro Arg Ala Gly
20 25 30

Val Leu Asn Ser Gln Ala Thr Asp Ser Tyr Gln Ser Thr Asp Tyr Tyr
35 40 45

Glu Pro His His Thr Gly Gly Gly Glu His
50 55

<210> 554

<211> 59

<212> PRT

<213> Homo sapiens

<400> 554

Leu Gln Lys Asn Lys Leu Arg Ala Ser Thr Asp Ser Thr Leu Trp Ile
 5 10 15
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 20 25 30
 Met Leu His Gly Gln Gly Leu Ala Leu Leu Ser Pro Thr Asn Leu Pro
 35 40 45
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 50 55

<210> 555
 <211> 71
 <212> PRT
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<400> 555
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 Pro Gln Leu Gly Ala Thr Ala Gln Gly Lys Val His Met Gly Leu Ser
 20 25 30
 Thr Ala Gln Gly Ser Ile Gln Asp Ile Lys Val Pro His Ser Ile Asp
 35 40 45
 Leu Val Ala Lys Lys Lys Lys Gln Thr Leu Ile Ser Phe Cys His Pro
 50 55 60
 Ser Asp Pro Leu Glu Leu Leu
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<210> 556
 <211> 81
 <212> PRT
 <213> Homo sapiens

<400> 556
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 20 25 30
 Arg Gln Ala Lys Glu Ala Ser Pro Val Leu Thr Ala Thr Arg His Gly
 35 40 45
 Ser Tyr Tyr Ser Leu Asn Ser Ala Ser Thr Gln Ile Ser Asp Asn Ile
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006330 "GCTGGA"

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<212> PRT
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<400> 559
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 Pro Arg
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<210> 560
 <211> 56
 <212> PRT
 <213> Homo sapiens
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 Glu Gly Ser Tyr Gly Thr Phe Tyr Cys Pro Arg Phe Tyr Thr Gly Tyr
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 35 40 45
 Thr Asp Leu Phe Leu Pro Pro Leu
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<210> 561
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 <212> PRT
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<220>
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 <222> (1)...(57)
 <223> Xaa = Any amino acid

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 Gly Leu Lys Ser Pro Glu Ile Lys Asn Pro Ala Pro Thr Gly Thr Ser
 20 25 30
 Asn Leu Ser Cys Phe Leu Ser Xaa Phe Trp Leu Met Gln Gly Thr Asn

006630 "SER" 560

35

40

45

Ser Leu Pro Arg Glu Asn Tyr Leu Asn
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<210> 562

<211> 59

<212> PRT

<213> Homo sapiens

<220>

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<222> (1)...(59)

<223> Xaa = Any amino acid

<400> 562

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Ala Pro Met His Gly Ile Lys Asn Ser Ile Thr Ser Leu Ile Phe Leu
 20 25 30

Ile Ser Tyr Leu Xaa Leu Glu Met Ser Ser Leu Ser Glu Ser Leu Val
 35 40 45

Leu Ser Ser Gly Asp Tyr Val Leu Asp Thr Pro
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<210> 563

<211> 79

<212> PRT

<213> Homo sapiens

<400> 563

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 5 10 15

Lys Gln Gln Pro Pro Ala Leu Ala Pro Gly His Pro Asp Phe Ile His
 20 25 30

Thr Gln Asn Glu Gln Ile Asp Pro Ser Pro His Ile Gln Asn Leu Met
 35 40 45

Trp Asn Pro His Leu Ser Gln Glu Leu Ala Glu Thr Phe Met Val Arg
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Asp Pro Leu Arg Pro Leu Leu Val Phe Ser Leu Ala Asp Ile Arg
 65 70 75

<210> 564

<211> 64

006630" SET 5960

<212> PRT
 <213> Homo sapiens

<400> 564
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 5 10 15
 Glu Arg Asp Gln Cys Leu Phe Leu Leu Leu Cys Tyr Gln Ile Tyr Thr
 20 25 30
 Val Arg His Leu Tyr Ile Leu Tyr Arg Thr Leu Gly Ser Arg Lys Ser
 35 40 45
 His Met Asn Leu Pro Leu Ser Ser Gly Ser Gln Leu Trp Leu Ala Pro
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<210> 565
 <211> 57
 <212> PRT
 <213> Homo sapiens
 <220>
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 <222> (1)...(57)
 <223> Xaa = Any amino acid

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 35 40 45
 Tyr Ala Val Ser Ser Xaa His Asn Val
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<210> 566
 <211> 55
 <212> PRT
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006230 "SERG60"

45

<400> 569


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<211> 951

<212> DNA

<213> Homo sapiens

<400> 570

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<212> DNA

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<212> DNA

<213> Homo sapiens

<400> 572

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cgccagtgtg ctggaattcg cccttagctc ggatccacta gtccagtgtg gtggaattcc 120
attgtgttgg gcccaacaca atggagccac cacatccagc ctgccacata cttttaaact 180
atcaggtctc atgagaactc atg 203

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<210> 573

<211> 132

<212> PRT

<213> Homo sapiens

<400> 573

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Met Val Glu Gly Glu Gly Glu Ala Arg His Val Leu His Gly Gly Arg
          5              10              15

Arg Glu Arg Val Arg Gly Glu Thr Ala Thr Asn Phe Phe Phe Leu Arg
          20              25              30

Gln Glu Ser Gly Pro Val Ala Gln Ala Gly Val Gln Trp His Asp Leu
          35              40              45

Ser Ser Leu Gln Pro Leu Pro His Arg Phe Lys Gln Phe Ser Cys Leu
          50              55              60

Ser Leu Pro His Ser Trp Asp His Arg Tyr Ala Pro Pro His Leu Ala
          65              70              75              80

Asn Phe Cys Ser Phe Ser Arg Asp Gly Val Ser Leu Cys Cys Ser Gly
          85              90              95

Trp Ser Lys Thr Pro Gly Leu Gln Gln Ser Ala Cys Leu Gly Leu Pro

```


100 105 110
 Lys Cys Trp Gly Tyr Arg His Lys Pro Pro His Pro Ala Cys His Ile
 115 120 125
 Leu Leu Asn Tyr
 130

<210> 574
 <211> 62
 <212> PRT
 <213> Homo sapiens

<400> 574
 Met Thr His Ser Ser Ala Trp Leu Glu Arg Pro Gln Glu Thr Tyr Asn
 5 10 15
 His Gly Gly Arg Arg Arg Gly Ser Lys Ala Arg Leu Thr Trp Trp Gln
 20 25 30
 Glu Arg Thr Ser Glu Gly Gly Asp Cys His Lys Leu Phe Phe Phe Glu
 35 40 45
 Thr Arg Val Trp Pro Cys Cys Pro Gly Trp Ser Ala Val Ala
 50 55 60

<210> 575
 <211> 76
 <212> PRT
 <213> Homo sapiens

<400> 575
 Met Val Lys Ser Arg Phe Thr Lys Asn Thr Lys Ile Thr Gln Ala Trp
 5 10 15
 Trp Arg Ala Pro Val Ile Pro Gly Thr Arg Glu Ala Glu Gly Gly Glu
 20 25 30
 Ser Leu Glu Pro Gly Arg Leu Arg Glu Glu Asn Arg Leu Asn Pro Gly
 35 40 45
 Gly Arg Gly Cys Ser Glu Pro Arg Ser Cys Cys Cys Thr Pro Ala Trp
 50 55 60
 Ser Thr Glu Gln Asp Ser Ala Ser Lys Thr Asn Lys
 65 70 75

<210> 576
 <211> 68
 <212> PRT
 <213> Homo sapiens

006220"3645960

<220>

<221> VARIANT

<222> (1)...(68)

<223> Xaa = Any Amino Acid

<400> 576

Met Leu Gly Lys Ser Arg Ala Val Cys Leu Pro Ser Thr Thr Val Thr
 5 10 15

Thr Val Cys Tyr Leu Ala Ser Ser Ser Ala Ser Arg Glu Thr Ala Thr
 20 25 30

Arg Gln Ala Pro Gly Asn Trp Lys Met Xaa Ser Lys Cys His Ala Gln
 35 40 45

Leu Leu Phe Thr Phe Tyr Leu Asn His Phe Tyr Gln Ile Arg Leu Asn
 50 55 60

Pro Gly Tyr Ser
 65

<210> 577

<211> 57

<212> PRT

<213> Homo sapiens

<400> 577

Met Tyr Leu Glu Asn Ser Phe Tyr Cys Gln Met Ile Leu Leu Lys Arg
 5 10 15

Cys Arg Leu Ser Lys Ile Ser Thr Gln Arg Val Val Pro Asp Gly Pro
 20 25 30

Pro Ala Pro Val Pro Gly Ser Phe Pro Met Phe Pro Arg Phe Gly Phe
 35 40 45

Arg Leu Ala Pro Pro Ala Asp Thr Pro
 50 55

<210> 578

<211> 51

<212> PRT

<213> Homo sapiens

<400> 578

Met Gln Leu Ile Tyr Leu Cys Phe Leu Gly Leu Leu Tyr Ile Arg His
 5 10 15

His Asp Ser Gln Ser Phe Val Ile Leu Tyr Tyr Lys Lys Leu Asn Tyr
 20 25 30

005230"3E2T5950

Tyr Phe Lys Tyr Gly Gln Ile Arg Ala Phe His Ile Ala Lys Val Tyr
 35 40 45

Gln Pro His
 50

<210> 579
 <211> 56
 <212> PRT
 <213> Homo sapiens

<400> 579
 Met His Phe Thr Phe Met Gln Leu Ile Tyr Leu Cys Phe Leu Gly Leu
 5 10 15

Leu Tyr Ile Arg His His Asp Ser Gln Ser Phe Val Ile Leu Tyr Tyr
 20 25 30

Lys Lys Leu Asn Tyr Tyr Phe Lys Tyr Gly Gln Ile Arg Ala Phe His
 35 40 45

Ile Ala Lys Val Tyr Gln Pro His
 50 55

<210> 580
 <211> 67
 <212> PRT
 <213> Homo sapiens

<400> 580
 Met Glu Leu Arg Thr Lys Ala Leu Arg Thr Ala Gln Gln Leu Thr Ser
 5 10 15

Cys Val Thr Ala Leu Lys Ala Ala Gly Pro Pro Leu Thr Phe Trp Lys
 20 25 30

Gly Lys Trp Val Gln Cys Cys Leu Pro Leu Trp Gly Leu Leu Gly Ser
 35 40 45

His Ala Phe Tyr Ile Tyr Ala Val Asp Ile Phe Met Phe Pro Gly Ser
 50 55 60

Phe Ile His
 65

<210> 581
 <211> 77
 <212> PRT
 <213> Homo sapiens

<400> 581

005230"364560

Met Leu Glu Val Lys Phe Glu Val Ser Leu Arg Pro Thr Gly Asn Glu
 5 10 15

Thr Ala Gly Gln Thr His Gly Thr Gln Asp Lys Gly Ser Lys Asp Ser
 20 25 30

Thr Ala Ala Asp Ile Leu Cys Asp Ser Leu Glu Ser Ser Arg Pro Ala
 35 40 45

Ala His Ile Leu Glu Gly Lys Met Gly Thr Met Leu Ser Ala Thr Leu
 50 55 60

Gly Pro Ser Trp Val Thr Cys Ile Leu His Leu Cys Ser
 65 70 75

<210> 582

<211> 51

<212> PRT

<213> Homo sapiens

<400> 582

Met Leu Phe Leu Gln Thr Ile Asp Thr Lys Cys Thr Gly Ile Glu Ile
 5 10 15

Asn Arg Asn Trp Ser Lys Val Trp His Thr His Ser His Val Asp Val
 20 25 30

Lys Leu Cys Leu Glu Phe Leu Cys Gly Val Trp Phe Gly Leu Gly Phe
 35 40 45

Leu Gly Val
 50

<210> 583

<211> 60

<212> PRT

<213> Homo sapiens

<400> 583

Met Ser Thr Ser Asp Gly Phe Ala Pro Pro Pro Gln Leu Gly Ser Arg
 5 10 15

Cys Ser His Ile Arg Gly Pro Ile Lys Ile Ala Arg Asn Lys Phe Pro
 20 25 30

Arg Thr Leu Thr Ser Gln Glu Leu Arg Arg Phe Ala Glu Tyr Ser Gly
 35 40 45

Met Met Phe Gly Asp Gln Thr Thr Ala Gly Gln Lys
 50 55 60

006230 "3625360

<210> 584
 <211> 76
 <212> PRT
 <213> Homo sapiens

<400> 584
 Met Cys Leu Cys Ile Pro Leu Gly Gly Tyr Gln Glu Leu Cys His Cys
 5 10 15
 Met Ser Thr Ser Asp Gly Phe Ala Pro Pro Pro Gln Leu Gly Ser Arg
 20 25 30
 Cys Ser His Ile Arg Gly Pro Ile Lys Ile Ala Arg Asn Lys Phe Pro
 35 40 45
 Arg Thr Leu Thr Ser Gln Glu Leu Arg Arg Phe Ala Glu Tyr Ser Gly
 50 55 60
 Met Met Phe Gly Asp Gln Thr Thr Ala Gly Gln Lys
 65 70 75

<210> 585
 <211> 50
 <212> PRT
 <213> Homo sapiens

<400> 585
 Met Val Tyr Arg Phe Gly Gln Met Ser Asp Asn Pro Phe Tyr Ile Leu
 5 10 15
 Ala Ser Leu Gly Ser Ser Ser Cys Arg Asn Gly Leu Ala Ser Lys Trp
 20 25 30
 Arg Gln Ala Asp Pro Ser Asp Gly Tyr Met Glu Pro Cys Phe Gln Leu
 35 40 45
 Leu Phe
 50

<210> 586
 <211> 60
 <212> PRT
 <213> Homo sapiens

<400> 586
 Met Leu Val His Ile Tyr Ser Cys Cys Gly Met Val Tyr Arg Phe Gly
 5 10 15
 Gln Met Ser Asp Asn Pro Phe Tyr Ile Leu Ala Ser Leu Gly Ser Ser
 20 25 30
 Ser Cys Arg Asn Gly Leu Ala Ser Lys Trp Arg Gln Ala Asp Pro Ser

35 40 45

Asp Gly Tyr Met Glu Pro Cys Phe Gln Leu Leu Phe
50 55 60

<210> 587
<211> 1408
<212> DNA
<213> Homo sapiens

<400> 587
ctggacactt tgcgagggct tttgctggct gctgctgctg cccgtcatgc tactcatcgt 60
agcccgcccg gtgaagctcg ctgctttccc tacctcctta agtgactgcc aaacgcccac 120
cggctggaat tgctctgggt atgatgacag agaaaatgat ctcttcctct gtgacaccaa 180
cacctgtaaa tttgatgggg aatgtttaag aattggagac actgtgactt gcgtctgtca 240
gttcaagtgc aacaatgact atgtgcctgt gtgtggctcc aatggggaga gctaccagaa 300
tgagtgttac ctgcgacagg ctgcatgcaa acagcagagt gagatacttg tgggtgtcaga 360
aggatcatgt gccacagatg caggatcagg atctggagat ggagtccatg aaggctctgg 420
agaaactagt caaaaggaga catccacctg tgatatttgc cagtttggtg cagaatgtga 480
cgaagatgcc gaggatgtct ggtgtgtgtg taatattgac tgttctcaaa ccaacttcaa 540
tcccctctgc gcttctgatg ggaaatctta tgataatgca tgccaaatca aagaagcatc 600
gtgtcagaaa caggagaaaa ttgaagtcac gtctttgggt cgatgtcaag ataacacaac 660
tacaactact aagtctgaag atgggcatta tgcaagaaca gattatgcag agaatgctaa 720
caaattagaa gaaagtgcc gagaacacca cataccttgt ccggaacatt acaatggctt 780
ctgcatgcat gggaagtgtg agcattctat caatatgcag gagccatctt gcaggtgtga 840
tgctggttat actggacaac actgtgaaaa aaaggactac agtgttctat acgttgttcc 900
cggctcctgta cgatttcagt atgtcttaac cgcagctgtg attggaacaa ttcagattgc 960
tgtcatctgt gtggtggtcc tctgcatcac aaggaaatgc ccagaagca acagaattca 1020
cagacagaag caaaatacac ggcactacag ttcagacaat acaacaagag cgtccacgag 1080
gttaattctaa agggagcatg tttcacagtg gctggactac cgagagcttg gactacacaa 1140
tacagtatta tagacaaaag aataagacaa gagatctaca catgttgcct tgcatttgtg 1200
gtaatctaca ccaatgaaaa catgtactac agctatattt gattatgtat ggatatattt 1260
gaaatagtat acattgtctt gatgtttttt ctgtaatgta aataaactat ttatatcaca 1320
caatawagtt ttttctttcc catgtatttg ttatatataa taaatactca gtgatgagaa 1380
aaaaaaaaa aaaaaaaaaa rwmgaccc 1408

<210> 588
<211> 81
<212> PRT
<213> Homo sapiens

<400> 588
Met Pro Gln Lys Gln Gln Asn Ser Gln Thr Glu Ala Lys Tyr Arg Ala
5 10 15
Leu Gln Phe Arg Gln Tyr Asn Lys Ser Val His Glu Val Asn Leu Lys
20 25 30
Gly Ala Cys Phe Thr Val Ala Gly Leu Pro Arg Ala Trp Thr Thr Gln
35 40 45
Tyr Ser Ile Ile Asp Lys Arg Ile Arg Gln Glu Ile Tyr Thr Cys Cys
50 55 60

Leu Ala Phe Val Val Ile Tyr Thr Asn Glu Asn Met Tyr Tyr Ser Tyr
 65 70 75 80

Ile

<210> 589
 <211> 157
 <212> PRT
 <213> Homo sapiens

<400> 589
 Met Thr Met Cys Leu Cys Val Ala Pro Met Gly Arg Ala Thr Arg Met
 5 10 15

Ser Val Thr Cys Asp Arg Leu His Ala Asn Ser Arg Val Arg Tyr Leu
 20 25 30

Trp Cys Gln Lys Asp His Val Pro Gln Met Gln Asp Gln Asp Leu Glu
 35 40 45

Met Glu Ser Met Lys Ala Leu Glu Lys Leu Val Lys Arg Arg His Pro
 50 55 60

Pro Val Ile Phe Ala Ser Leu Val Gln Asn Val Thr Lys Met Pro Arg
 65 70 75 80

Met Ser Gly Val Cys Val Ile Leu Thr Val Leu Lys Pro Thr Ser Ile
 85 90 95

Pro Ser Ala Leu Leu Met Gly Asn Leu Met Ile Met His Ala Lys Ser
 100 105 110

Lys Lys His Arg Val Arg Asn Arg Arg Lys Leu Lys Ser Cys Leu Trp
 115 120 125

Val Asp Val Lys Ile Thr Gln Leu Gln Leu Leu Ser Leu Lys Met Gly
 130 135 140

Ile Met Gln Glu Gln Ile Met Gln Arg Met Leu Thr Asn
 145 150 155

<210> 590
 <211> 347
 <212> PRT
 <213> Homo sapiens

<400> 590
 Met Leu Leu Ile Val Ala Arg Pro Val Lys Leu Ala Ala Phe Pro Thr
 5 10 15

005230 "347560

Ser Leu Ser Asp Cys Gln Thr Pro Thr Gly Trp Asn Cys Ser Gly Tyr
 20 25 30
 Asp Asp Arg Glu Asn Asp Leu Phe Leu Cys Asp Thr Asn Thr Cys Lys
 35 40 45
 Phe Asp Gly Glu Cys Leu Arg Ile Gly Asp Thr Val Thr Cys Val Cys
 50 55 60
 Gln Phe Lys Cys Asn Asn Asp Tyr Val Pro Val Cys Gly Ser Asn Gly
 65 70 75 80
 Glu Ser Tyr Gln Asn Glu Cys Tyr Leu Arg Gln Ala Ala Cys Lys Gln
 85 90 95
 Gln Ser Glu Ile Leu Val Val Ser Glu Gly Ser Cys Ala Thr Asp Ala
 100 105 110
 Gly Ser Gly Ser Gly Asp Gly Val His Glu Gly Ser Gly Glu Thr Ser
 115 120 125
 Gln Lys Glu Thr Ser Thr Cys Asp Ile Cys Gln Phe Gly Ala Glu Cys
 130 135 140
 Asp Glu Asp Ala Glu Asp Val Trp Cys Val Cys Asn Ile Asp Cys Ser
 145 150 155 160
 Gln Thr Asn Phe Asn Pro Leu Cys Ala Ser Asp Gly Lys Ser Tyr Asp
 165 170 175
 Asn Ala Cys Gln Ile Lys Glu Ala Ser Cys Gln Lys Gln Glu Lys Ile
 180 185 190
 Glu Val Met Ser Leu Gly Arg Cys Gln Asp Asn Thr Thr Thr Thr Thr
 195 200 205
 Lys Ser Glu Asp Gly His Tyr Ala Arg Thr Asp Tyr Ala Glu Asn Ala
 210 215 220
 Asn Lys Leu Glu Glu Ser Ala Arg Glu His His Ile Pro Cys Pro Glu
 225 230 235 240
 His Tyr Asn Gly Phe Cys Met His Gly Lys Cys Glu His Ser Ile Asn
 245 250 255
 Met Gln Glu Pro Ser Cys Arg Cys Asp Ala Gly Tyr Thr Gly Gln His
 260 265 270
 Cys Glu Lys Lys Asp Tyr Ser Val Leu Tyr Val Val Pro Gly Pro Val
 275 280 285
 Arg Phe Gln Tyr Val Leu Ile Ala Ala Val Ile Gly Thr Ile Gln Ile
 290 295 300

005533.052500

Ala Val Ile Cys Val Val Val Leu Cys Ile Thr Arg Lys Cys Pro Arg
305 310 315 320

Ser Asn Arg Ile His Arg Gln Lys Gln Asn Thr Gly His Tyr Ser Ser
325 330 335

Asp Asn Thr Thr Arg Ala Ser Thr Arg Leu Ile
340 345

<210> 591

<211> 565

<212> DNA

<213> Homo sapien

<400> 591

actaaagcaa	atgaacaagc	tgacttgcta	gtatcatctg	cattcattga	agcacaagaa	60
cttcatgcct	tgactcatgt	aaatgcaata	ggattaaaaa	ataaatttga	tatcacatgg	120
aaacagacaa	aaaatattgt	acaacattgc	acccagtgtc	agattctaca	cctggccact	180
caggaagcaa	gagttaatcc	cagaggtcta	tgctctaata	tgttatggca	aatggatgtc	240
atgcacgtac	cttcatttgg	aaaattgtca	tttgtccatg	tgacagttga	tacttattca	300
catttcatat	gggcaacctg	ccagacagga	gaaagtactt	cccatgttaa	aagacattta	360
ttatcttgtt	ttcctgtcat	gggagttcca	gaaaaagtta	aaacagacaa	tgggccaggt	420
tactgtagta	aagcatttca	aaaattctta	aatcagtggg	aaattacaca	tacaatagga	480
attctctata	attcccaagg	acaggccata	attgaaggaa	ctaatagaac	actcaaagct	540
caattggtta	aacaaaaaaaa	aaaaa				565

<210> 592

<211> 188

<212> PRT

<213> Homo sapien

<400> 592

Thr	Lys	Ala	Asn	Glu	Gln	Ala	Asp	Leu	Leu	Val	Ser	Ser	Ala	Phe	Ile
1			5					10					15		
Glu	Ala	Gln	Glu	Leu	His	Ala	Leu	Thr	His	Val	Asn	Ala	Ile	Gly	Leu
		20						25				30			
Lys	Asn	Lys	Phe	Asp	Ile	Thr	Trp	Lys	Gln	Thr	Lys	Asn	Ile	Val	Gln
	35						40				45				
His	Cys	Thr	Gln	Cys	Gln	Ile	Leu	His	Leu	Ala	Thr	Gln	Glu	Ala	Arg
	50					55				60					
Val	Asn	Pro	Arg	Gly	Leu	Cys	Pro	Asn	Val	Leu	Trp	Gln	Met	Asp	Val
65					70					75				80	
Met	His	Val	Pro	Ser	Phe	Gly	Lys	Leu	Ser	Phe	Val	His	Val	Thr	Val
			85					90					95		
Asp	Thr	Tyr	Ser	His	Phe	Ile	Trp	Ala	Thr	Cys	Gln	Thr	Gly	Glu	Ser
		100					105					110			
Thr	Ser	His	Val	Lys	Arg	His	Leu	Leu	Ser	Cys	Phe	Pro	Val	Met	Gly
	115						120					125			
Val	Pro	Glu	Lys	Val	Lys	Thr	Asp	Asn	Gly	Pro	Gly	Tyr	Cys	Ser	Lys
	130					135				140					
Ala	Phe	Gln	Lys	Phe	Leu	Asn	Gln	Trp	Lys	Ile	Thr	His	Thr	Ile	Gly
145					150				155					160	

Ile Leu Tyr Asn Ser Gln Gly Gln Ala Ile Ile Glu Gly Thr Asn Arg
 165 170 175
 Thr Leu Lys Ala Gln Leu Val Lys Gln Lys Lys Lys
 180 185

<210> 593
 <211> 271
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(271)
 <223> n = A,T,C or G

<400> 593
 actttatgtt cnagtgcana aancncctg gattgccacc ntactctcag ggctgtgant 60
 tgtgcnccca nagcaacctg ggcacgcggg gacagggggg ccnacaattg agggagcggg 120
 gtccctagct ggggtctata catgncnggg naagggcngc tgagtnccat nagcaaagga 180
 nctagnatnt gcgggggtgc ggcctggggc taccctttna agcatccntn gatccactcc 240
 angaancng gggtagncag gtttnccaac a 271

<210> 594
 <211> 376
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(376)
 <223> n = A,T,C or G

<400> 594
 cctttggggg nggggggaac ctttaccatt gtnccccttt atttcatttg gttnggggtc 60
 gcgcctctnn gggccaacaa agttatcgtn nttgaagaga anattttttt ggnttngncc 120
 cgattaagcg ncaaattgtg agcaaaangc cgtgccactt gtggcgtagc tncgtcgggt 180
 cgattcgacg acaaggcgtn gcgcgntanc gttagtctcn aatngaccen gtggcatgag 240
 cccacgangg ntctgtgtcg tcacatggnc tctagacata acgcncncn ttttttncag 300
 agggggntgc cgcccttagg gaggnagggg tggggacact agccaancca nantctnacc 360
 ccattgaaga aaaggn 376

<210> 595
 <211> 242
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(242)
 <223> n = A,T,C or G

<400> 595
 agnctgctgn tcgtnccctn tatgtggctt catnntgagg acaanagtng cactgaggct 60
 tgngnatgcc aggcaaggnc aagctggctc aaaaagcatc caccacctc tgnaangggg 120

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<210> 596
<211> 535
<212> DNA
<213> Homo sapien
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<400>	596						
accagttgga	tactgctaaa	nagatatatta	tgcagcctca	tatgttaagt	cgtatatttt		60
gaaagctttt	taaatttttt	ctttaagaag	attttagatg	cttatcactg	agtaccagag		120
ggatgtaggc	tgatgccctt	atcaacaaag	tcagggactg	tggcacacaa	ggattgacta		180
ctgcagacac	ggccacaatg	ctacctctag	agggcctgaa	tccccctgcc	ctctctgggtg		240
gggagaaggg	ctggcagagc	cattagcatg	ggctccggcc	aatcctggcc	actttgacac		300
tcttggtgct	gaccagggtt	cctggaggaa	gggatgaggt	gggcagtaga	gatgctcagg		360
gcagtggccc	ctttccatcc	acactggaac	tatttcagta	ttttaccacc	aattcagcca		420
ttcccttggtg	cgctggctga	acatcagccc	tgctccaggt	ctcagtttcc	cctttgtaaa		480
gggaaagctc	tggattcagg	gagtgatgaa	gaggtcatca	tgggtcttgag	aattc		535

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<220>
<221> misc_feature
<222> (1)...(257)
<223> n = A,T,C or G
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<210> 598
<211> 222
<212> DNA
<213> Homo sapien
```

<400> 598
nntggntacc gtcnaaaactt nncttggtac ccgagctcgg atccactagt ccagtgtggt 60

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ggaattccat tgtgttgggc tataagctgt aatagtggag nctgtctngg ttcattgcan 120
nagnccctcc gcanncaacn ttgnnacaac ctgtgagnag gcnataaatt attcacataa 180
tcatcactgc atgaanctga ctcaaacgca tccacntaca cc 222

```

```

<210> 599
<211> 238
<212> DNA
<213> Homo sapien

```

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<220>
<221> misc_feature
<222> (1)...(238)
<223> n = A,T,C or G

```

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<400> 599
gcatgacatc ancgatgtnt ttggnnacct ganattngct aaaactngng natgccgggn 60
atgnaggttt ggtantgatc tatgcaactca catctcatgg ggacgtttca tgtggagtgn 120
tcgacaangt tgctgnancn gagaagtgat gatctcagtt gaaaggggtca tgtgaataca 180
cnttacactt gaaaaagaag cacattggga atatcacgaa acgnccacca acatcctg 238

```

```

<210> 600
<211> 232
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(232)
<223> n = A,T,C or G

```

```

<400> 600
cgaactatatt agactaccta ggaaaattat tttagtatca gaagaatatc aggggtgtag 60
tactcatcag agctaaatga gagcgcttta aaaatgttag tttgtcttcc gccatttcta 120
cagaaagctg caatttcagg tttcaacct aataggtgat atttaanaaa aaaaaaagc 180
aatcgcaaat agccccactg cttttacaaa tcattttttc cccaacacaa tg 232

```

```

<210> 601
<211> 547
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(547)
<223> n = A,T,C or G

```

```

<400> 601
cattgtgttg gggaaaaaat gatttgtata agcagtgggg ctatttgcca ttgctttttt 60
tttttcttaa atatcaccta ttaggttgaa aacctgaaat tgcagctttc tgtagaatg 120
gcggaagaca aactaacatt tttaaagcgc tctcatttag ctctgatgag tactacaccc 180
ctnatattct tctgatacta aaataatttt cctagtgtag tctaaacttt tttaaaaaga 240
catgtaatcc gcggagttag taactcaaaa cgagtgcac tnggaagtat cgcagccggt 300
nctggatnaa attcccagct tgctngcttg ctnagccggg gggcggtnaa aaaaacatct 360
gcagcccnng ggnaaaaacc ttgcattgt tcttacgtgt ttacgttatt ttatttcctt 420

```

nnagcaaggc nggganttgg ggactcgaaa tggtagagtt gggctgggga tcgcccttgt 480
 tacataaaaag ncgtccagaa gagggacggg tacaggcnng ganctccaaa ggtagtccc 540
 tgccatt 547

<210> 602
 <211> 826
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(826)
 <223> n = A,T,C or G

<400> 602
 cgggggggnt tacgtctctc tggacgcttt tattgtacca gggcgatccc agcccaactg 60
 taccattcga gtccctactc ctgccttgct ctagggaat aaaataacgt aaacacgtaa 120
 gaacaatgcg aaagcgcttt ctccctagg ctgcagattg tcttcttcac cgcccctgct 180
 tagtagcta gctagctggg aatttaatcc agaaacggct tgcgatacct cctagatgca 240
 ctcgttttga gttacaaact ccgcggtatta catgtctttt taaaaaagtt tagactacac 300
 tagggaaaat tatttttagta tcagaagaat atcagggggg gtagtactca tcagagctna 360
 atgagagcgc tttaaaaatg ttagtttgct ttccgccatt tctacagaaa gctgcaattt 420
 caggttttca ncctaataagg tgatatntaa gaaaaaaaaa acaatcgcan atagcccact 480
 gcttttacaa atcatttttct tcttctagggt atagcctgtc aggtggccta atgtattttt 540
 gacatctcta ggaattttta tagaccagaa atgggtgcca gagatatgcc tgcactaatc 600
 ttaagtgggg atttatgtat ttctcaanca agtgattaaa gcaaaactag gcacgaatga 660
 aatcaagatc tttaggccag aaatcatgaa nanttttana attattttan gaatctgtgg 720
 cttctcttct taaaatngaa aaaaaaattg tttaaacca naaggtctga ataccaagc 780
 nccctgaacn anagaacaan gccggagcac cccctcccaa atcccc 826

<210> 603
 <211> 817
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(817)
 <223> n = A,T,C or G

<400> 603
 nnangacttt tgtggtntta tacaattntt ttttctattt ctatgaagag aaagccacag 60
 agtcctaaaa taattctaaa actcatcatg actttcttgc ctaaaagatc ttgatttcaa 120
 tcgtgcctag ttttgcttta atcacttgct tgagaaatac ataaatcccc acttaagatt 180
 agtgcaggca tatctctggc acccatttct ggttctatta aaattcctag agatgtcaaa 240
 aattacatta ggccacctga caggctatac ctagaagaga aaaaatgatt tgtaaaagca 300
 gtggggctat ttgcgattgc tttttttttt tcttaaatat cacctattag gttgaaaacc 360
 tgaaattgca gctttctgta gaaatggcgg aagacaaact aacattttta aagcgtctct 420
 atttagctct gatgagtact acaccctga tattcttctg atactaaaat aattttccta 480
 gtgtagtcta aactttttta aaaagacatg taatccgcgg agtttgtaac tcaaaacgag 540
 tgcacttagg aggtatcgca agccgtttct ggattaaatt ccagctagc ttgcttgctt 600
 agcaggggcg ggnaaanaag acatctgcag cctagggaag aaaacctttc gcattgttct 660
 tacgtgttta cgttatttta tttcctanaa caaggcnгаа ttgggactcg aatgggtcag 720
 ttgggggtggg ggatcccctg gtncataaaa ngtcanaaag anggtacagg cggaacncca 780

817

```
<220>  
<221> misc_feature  
<222> (1)...(694)  
<223> n = A,T,C or G
```

```
<210> 605
<211> 678
<212> DNA
<213> Homo sapien
```

[illegible]

```
<210> 606
<211> 263
<212> DNA
<213> Homo sapien
```

<220>
 <221> misc_feature
 <222> (1)...(263)
 <223> n = A,T,C or G

<400> 606
 gtgggggtcng cancagccaa ctcagcttcc tttcgggctt tgtagcaga cggatcatcc 60
 tctagtccac tgtgntcaaa ttccattgtg tggggggcnc tcgcctcggc canagatctg 120
 agtgancana cntgtcccca ctgaggtgcc ccacagcngn ttgtnttcag cangggctna 180
 caactcgacc ggcagcgan ggctggcaga antgngcgcc tnnctcattc ctacgcngtn 240
 ngccgcagga aggangacag gcc 263

<210> 607
 <211> 22
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Primer

<400> 607
 ccatgtgggt cccggttgtc tt 22

<210> 608
 <211> 22
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Primer

<400> 608
 gataggggtg ctcaggggtt gg 22

<210> 609
 <211> 40
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Primer

<400> 609
 gctggacagg gggcaaaagc tggggcagtg aaccatgtgc 40

<210> 610
 <211> 27
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Primer

006230 "AETG60"

<400> 610
 ccttgtccag atagcccagt agctgac 27

<210> 611
 <211> 46
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Primer

<400> 611
 gatagagaaa accgtccagg ccagtattgt gggaggctgg gagtgc 46

<210> 612
 <211> 40
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Primer

<400> 612
 gcacatggtt cactgcccc a gcttttgccc cctgtccagc 40

<210> 613
 <211> 38
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Primer

<400> 613
 gccgctcgag ttagaattcg gggttggcca cgatgggtg 38

<210> 614
 <211> 53
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Primer

<400> 614
 cggcgggcat atgcatcacc atcaccatca catcataaac ggcgaggact gca 53

<210> 615
 <211> 46
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Primer

<400> 615
gcactcccag cctcccacaa tactggcctg gacgggttttc tctatc

46

<210> 616
<211> 1350
<212> DNA
<213> Homo sapien

<400> 616
atgcatcacc atcaccatca catcataaac ggcgaggact gcagcccgca ctgcagccc 60
tggcaggcgg cactggatcat ggaaaacgaa ttgttctgct cgggcgtcct ggtgcatccg 120
cagtgggtgc tgtcagccgc acactgtttc cagaactcct acaccatcgg gctgggcctg 180
cacagtcttg aggcgcacca agagccaggg agccagatgg tggaggccag cctctccgta 240
cggcaccag agtacaacag acccttgctc gctaacgacc tcatgctcat caagttggac 300
gaatccgtgt ccgagtctga caccatccgg agcatcagca ttgcttcgca gtgccctacc 360
gcggggaact cttgcctcgt ttctggctgg ggtctgctgg cgaacggcag aatgcctacc 420
gtgctgcagt gcgtgaacgt gtccgtgggtg tctgaggagg tctgcagtaa gctctatgac 480
ccgtgtgacc accccagcat gttctgcgcc ggcggaggggc aagaccagaa ggactcctgc 540
aacggtgact ctgggggggcc cctgatctgc aacgggtact tgcagggcct tgtgtctttc 600
ggaaaagccc cgtgtggcca agttggcgtg ccagggtgtct acaccaacct ctgcaaattc 660
actgagtgga tagagaaaac cgtccaggcc agtattgtgg gaggctggga gtgcgagaag 720
cattcccaac cctggcagggt gcttgtggcc tctcgtggca gggcagctctg cggcgggtgtt 780
ctggtgcacc cccagtgggt cctcacagct gccactgca tcaggaacaa aagcgtgatc 840
ttgctgggtc ggcacagcct gtttcatcct gaagacacag gccagggtatt tcaggtcagc 900
cacagcttcc cacaccgcgt ctacgatatg agcctcctga agaatcgatt cctcaggcca 960
ggtgatgact ccagccacga cctcatgctg ctccgcctgt cagagcctgc cgagctcacg 1020
gatgctgtga aggtcatgga cctgcccacc caggagccag cactggggac cacctgctac 1080
gcctcaggct ggggcagcat tgaaccagag gagttcttga ccccaaagaa acttcagtgt 1140
gtggacctcc atgttatatt caatgacgtg tgtgcgcaag ttcacctca gaaggtgacc 1200
aagttcatgc tgtgtgctgg acgctggaca gggggcaaaa gctggggcag tgaacctgt 1260
gccctgcccg aaaggccttc cctgtacacc aagggtggtgc attaccggaa gtggatcaag 1320
gacaccatcg tggccaaccc cgaattctaa 1350

<210> 617
<211> 449
<212> PRT
<213> Homo sapien

<400> 617
Met His His His His His Ile Ile Asn Gly Glu Asp Cys Ser Pro
1 5 10 15
His Ser Gln Pro Trp Gln Ala Ala Leu Val Met Glu Asn Glu Leu Phe
20 25 30
Cys Ser Gly Val Leu Val His Pro Gln Trp Val Leu Ser Ala Ala His
35 40 45
Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu Gly Leu His Ser Leu Glu
50 55 60
Ala Asp Gln Glu Pro Gly Ser Gln Met Val Glu Ala Ser Leu Ser Val
65 70 75 80
Arg His Pro Glu Tyr Asn Arg Pro Leu Leu Ala Asn Asp Leu Met Leu
85 90 95
Ile Lys Leu Asp Glu Ser Val Ser Glu Ser Asp Thr Ile Arg Ser Ile
100 105 110

```

Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly Asn Ser Cys Leu Val Ser
      115              120              125
Gly Trp Gly Leu Leu Ala Asn Gly Arg Met Pro Thr Val Leu Gln Cys
      130              135              140
Val Asn Val Ser Val Val Ser Glu Glu Val Cys Ser Lys Leu Tyr Asp
      145              150              155              160
Pro Leu Tyr His Pro Ser Met Phe Cys Ala Gly Gly Gly Gln Asp Gln
      165              170              175
Lys Asp Ser Cys Asn Gly Asp Ser Gly Gly Pro Leu Ile Cys Asn Gly
      180              185              190
Tyr Leu Gln Gly Leu Val Ser Phe Gly Lys Ala Pro Cys Gly Gln Val
      195              200              205
Gly Val Pro Gly Val Tyr Thr Asn Leu Cys Lys Phe Thr Glu Trp Ile
      210              215              220
Glu Lys Thr Val Gln Ala Ser Ile Val Gly Gly Trp Glu Cys Glu Lys
      225              230              235              240
His Ser Gln Pro Trp Gln Val Leu Val Ala Ser Arg Gly Arg Ala Val
      245              250              255
Cys Gly Gly Val Leu Val His Pro Gln Trp Val Leu Thr Ala Ala His
      260              265              270
Cys Ile Arg Asn Lys Ser Val Ile Leu Leu Gly Arg His Ser Leu Phe
      275              280              285
His Pro Glu Asp Thr Gly Gln Val Phe Gln Val Ser His Ser Phe Pro
      290              295              300
His Pro Leu Tyr Asp Met Ser Leu Leu Lys Asn Arg Phe Leu Arg Pro
      305              310              315              320
Gly Asp Asp Ser Ser His Asp Leu Met Leu Leu Arg Leu Ser Glu Pro
      325              330              335
Ala Glu Leu Thr Asp Ala Val Lys Val Met Asp Leu Pro Thr Gln Glu
      340              345              350
Pro Ala Leu Gly Thr Thr Cys Tyr Ala Ser Gly Trp Gly Ser Ile Glu
      355              360              365
Pro Glu Glu Phe Leu Thr Pro Lys Lys Leu Gln Cys Val Asp Leu His
      370              375              380
Val Ile Ser Asn Asp Val Cys Ala Gln Val His Pro Gln Lys Val Thr
      385              390              395              400
Lys Phe Met Leu Cys Ala Gly Arg Trp Thr Gly Gly Lys Ser Trp Gly
      405              410              415
Ser Glu Pro Cys Ala Leu Pro Glu Arg Pro Ser Leu Tyr Thr Lys Val
      420              425              430
Val His Tyr Arg Lys Trp Ile Lys Asp Thr Ile Val Ala Asn Pro Glu
      435              440              445
Phe

```

<210> 618

<211> 385

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(385)

<223> n = A,T,C or G

```

<400> 618
ctgtgctgag aacccaaaagc tatgancact gctttttccaa atgtccataa naccaacatt      60
tttatcacta ccaccatcac ctgggagctc nttagaaagc tagtctcccg ggcaccaccc      120
tggcctactg aacctaattgt gcattttaaca agattnacgt ngaaatctgc aaagcacagg      180
ggcngataac agtaccacct gntctggttc ctanccccc an gacccttaca gtctaactgg      240
gacacaaggg cttnaaatca aattgcctat cattaagata tacaanganc ntgagaaact      300
gctncactta tntattaagg ngctctaaga cttagaaacn aaangcantg ctgagangat      360
tcaaatatga ngggggncac tttnc                                           385

```

<210> 619

<211> 869

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(869)

<223> n = A,T,C or G

```

<400> 619
gatatcccgga gaattcgagg ccgcgtcgac ctctacttgt ttagacataa atgcagtcta      60
gcattaaaga tccttttaaaa aaatgttttc ccaatgggta aaagacaagc tcaataaat      120
gaactctcat acatatgcca aaattgatga gtagataaat atttcagtag gtagtacta      180
gctttctgtg tatgagtaaa catatgggag aaatttaaaa cactaaagta gactcaatga      240
aagcatagta toctatgtat tcgtttttca gaaatgtcta atgaaggaag gaaacaatga      300
atgaatgccc ttattcctct tagagtgtcg ggacatgggt ttgcctgaaa acttcatgtg      360
aattttatat tttgctacac attacaccca tcttagactt atacgtataa gacataaggc      420
atatcttatg tcttacatgt ataataatct aagcagaaca aaaaataacg aaataatttc      480
ttcccccatt ttttgagaca gatggatttt ccggaaagat gtgttttagct tttaatcctg      540
tgggtttgtg taccacctgg cacactagag tgttgctcta attcagtgag ttgtaactct      600
gggtgaacag tggaataact aggggtacatt ttaaaaaatgc taatgctcgg gcctcgctga      660
agaccaaatt aattggaatc tctgngggng gnattgatct ttttataatc tttctanang      720
attctaattg gcttccaggg atgaaaaccn ctgntggagc tnggaacott cctttagttt      780
ggagaaaccc cgatgagggt ntnttaggcn ccgcctnttt ttggcctggg cttccccccc      840
tatntntttt tggaanggnc cnaattttt                                           869

```

<210> 620

<211> 339

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(339)

<223> n = A,T,C or G

```

<400> 620
gngcgggcct cncctgtgct gctctcgctg ccgaagctct ttttccacca gctgtaggan      60
aagcccgaag accactgggc ccccggttag cccaagtacc actgggtctc ctggctcctg      120
acgctnccgg tcttctcgtg ggcgtagact gccagcttcg gagaccctc agccctcccc      180
cgctttttct caccacagga ggccatcagt agcgagctac tgctcgggcc acaacctccc      240
agcangatag cccgcgggtt ccaatctgcg aaaggaggac cgccnagccc gaaatgccna      300
gcccgcnat cactgccacg ccgagccnag cgctcgtgc                                           339

```

<210> 621
 <211> 267
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(267)
 <223> n = A,T,C or G

<400> 621
 gggngcatg gtccnngta gccaaagtaca tggctcctcct ggctcctgac gctacggggtc 60
 ttctctcgtgg cgtagactgc cagcttcgga gacctctcag cccctccccg cttttctcca 120
 cccaggagg ccatcagtag cgagctactg cctcggccac aacctcccag caggatngcc 180
 cgcggtttcc aatctgcgaa aggaggaccg ccnagccaga aatgccnagc cnagcgatca 240
 ctgccacgcc nagccnagcg ctctgtgc 267

<210> 622
 <211> 847
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(847)
 <223> n = A,T,C or G

<400> 622
 cttangntgt cgactgacgt catgcatgan ttaaagcaga ggtttggtga aatttatgaa 60
 aaatacaaaa ttccggccttg tcttgaggaa gagccactac ttgataactc tacaagagga 120
 acagatgtga aggatattcc ctttaatttg acaaataaca tacctgggtg tgaggaagaa 180
 gatgcatctg aaatatctgt ctcaagtggta ttcgagacat ttctgaaca aaaagaaccc 240
 agtctcaaaa atatcatcca tccatactat catccgtact ctgggtccca ggaacatggt 300
 tgccagtcac cttctaagct tcattttacat gaaaataaat tagactgcga caatgataac 360
 aaactaggca ttggacatat ttttagtaca gataacaact ttcataatga tgcaagcact 420
 aagaaagcaa ggaaccacga agtggttacg gttgaaatga aagaagacca agagtttgat 480
 ttgcaaatga caaaaaatat gaaccaaaat agtgacagtg gcagtacaaa taactataaa 540
 agcctgaaac cttaaattaga aaatctgagt tctttaccac cagattctga cagaacatca 600
 ggaagtatat ctacatgaag aattacagca agacatgcc aagttttaag aatgangtca 660
 acacattaga aanaagantt ctgggctttg aagaaagaaa atgttccact tcataaagaa 720
 ggttgaaaga agaatgggag agccnngaan tttttgccn gaaattttcg ggaaccctac 780
 tggatgggtc nactggttgg ccatgaatga ataatggact aatcnnccaa ttctnngga 840
 agggaat 847

<210> 623
 <211> 681
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(681)
 <223> n = A,T,C or G

```

<400> 623
aaaactgtac tcgcgcgctg catgtcgaca ctagtggatc caaagaatcg gcacgagcga      60
aaangctcan gcagcccggc tggccgccgc cgctcctccc cccaggaaag ccaangtgga      120
ngctgatgtg gctgcangag ctcgtttcac agccccctcan gtgganctgg ttggggccgcg      180
gctgccangg gcggaagtgg gtgtccccan gtctcagccc caaggetgcc cctcaciaaag      240
cactgggtgt ttgcctccac tgccaccttg ggctccgaac ccgctccccct gctgtggang      300
cccaccgtgg gaatccaggt cccaggtgg actgcctgcc ttgccctcac tgcccactct      360
gcccacactt ccctgcctag anaccgggaa ggggctgtgt cggtantggt gcccacctgg      420
atgtggcagc accgactgtg ggggtggacc tggccttgcc gggtgcaaaa gtggggggccc      480
ngggaaaagc acctgaagtg gccctgaaaa atccccctt aattttnccc caatttgggg      540
ctcnaacaaa aggaaattgc tgaagccaan ggtaccaagg tcacccctaa ggccagggtg      600
aaaagggtccc aaaattccaa tnccacacnt ttgggcttnc ctcttggaac cccggcccc      660
tctcntgaan ttttaaaaaa n                                           681

```

<210> 624

<211> 661

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(661)

<223> n = A,T,C or G

```

<400> 624
attggtctta ctgtaccacc ggggtggaaat cgatggccgc ggcgctctaaa tatccgattt      60
tttttttttt tcctcttctg actgtccatg gacaaatgaa actaacttaa tctaactaaa      120
aaacacaact atattttgaa gatttttctat ctgcactcaa ggacactttc cacnccggtt      180
ttgttacctt ttggtcttgt ctctgaacat gaaattnatc tcaagggatt ngatttctgg      240
acctcctatt cctgctatgg gtttgatatt tcttgggctc cagggccact gttgcattgg      300
gntgacagnt acctcctagc ccatanccct ctatcttggg aaacaaacct aacaactacg      360
tgtaccttcc atagatctct gattgagtct cagtatnccg ttgctcatgg gcgattcact      420
tgaatccgtn attggtgcca acaatcctga ctcatggggnn aatggatcct atcacgttcc      480
cctgattngc aaccctgta tacatanatc taatcgcata gaatctagcn tnggntatgc      540
gcggctacgc tatcagggnt tgntaactat ngcatggcta cgaancctga tcatgatcna      600
gggtcatgga ctcttatcag ggggggttggg ccgngcttct ttttcnnacc ttggtaaaac      660
c                                           661

```

<210> 625

<211> 181

<212> DNA

<213> Homo sapien

<400> 625

```

gcaacaatca gatcatgtta aagtaaattct ccattgccct ggatcacttc aggatttaat      60
tgtccaagga gagcagggtt ctctgtgaa aaaaagggtg ggaaatgttt gagagtaaaa      120
aatacaaaat tcaaccgggtc gaaaatacac cactccattc agtgcctctac ccccataagc      180
c                                           181

```

<210> 626

<211> 181

<212> DNA

<213> Homo sapien

<400> 626
gcaacaatca gatcatgtta aagtaaatct ccattgccct ggatcacttc aggatttaat 60
tgtccaagga gagcaggggt ctctgtgaa aaaaagggtg ggaaatgttt gagagtaaaa 120
aatacaaaat tcaaccggtc gaaaatacac cactccattc agtgctctac ccccataagc 180
c 181

<210> 627
<211> 813
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(813)
<223> n = A,T,C or G

<400> 627
accaagctgg agctcgcgcg cctgcaggtc gacactagtg gatccaaagt gaacgtgaag 60
gtgagcagag gagaacttgc gatggcaaag ttaaaaacaa gaggagatga tggctctgggt 120
gtggcacagg atgttaaaaa aattctcctg tccttaagga gttactgcta tttgagtaat 180
gtgccacttc cctacatagc cttctatgca gaaatgctat atttcactt cacaaccag 240
aacgtgcatt ttatttttaca tttagaggag gaacaaacaa ccagaaggca aaaactggtg 300
cattatTTTT tgcaattctc ttggaaagag ttcgTTTTta acttctgctc agacagcaca 360
caactactgg gaatatattt taatttcaaa tctgatgtgt gacatctggt aactcattta 420
ttgctaataga agttttcaca ggaagcagca gtcaccagta gctcatctta tttttcagtt 480
ggcaaagtgt tgtttacctt ttattggcct gcacgggtgt ctcttatcac aggatattta 540
attagaaaac gcaagtagcc taacatagaa nagaaatgga gtggtagata atagtagata 600
gaatggctaa atatttttat tacagtgatg taatatcact gnaatttatg gttaaaaatt 660
atgtaatact caaaaaggaat tctcagactg gcgaaacagc tggnaacag ctntcacagg 720
gctttanact cctnttgagc tttccccctg ntggacttta gtcttccttt tacncccgna 780
gttnccattn nttaccaatt gtnccgggaa ana 813

<210> 628
<211> 646
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(646)
<223> n = A,T,C or G

<400> 628
tttggngngn ggtgtctcnt ttgggtggac tttttgggtc gtagggcccc aaggccgtta 60
atcccgtaat aacggaagac gaagaagagt cagaagagtg cttctataag gatcgggacg 120
agactacctt agaggaataa aggaaaaaag cagaggagga agagtggtag aaggagtcag 180
aagaaaccca cacgtcgttc tgaacctgga gccttatcaa aaaggtctag ataaacgata 240
gcatctcga tatcgagctc aagaggtagg tttagagact tctcgctcctc gagagcgaaa 300
tggaagatct cgacgacgat aagaagttaa agtgtagagg gtgcttgagg agcgcgtgga 360
aggattctgc ggagggaccc atcgacgtag agacttgaag gcctactaag gtccacaaga 420
agcccggtc tttctccgaa tggctgggagc gtacagtatg cgacgtcgat cggcagacaa 480
gctggcggtg gactcgaagt gttcgggcga atcgacttat aatagtcgag cgctagtaac 540
gtaggaacac gaagagtagt cgaaagaaaa cgttttagtga gggaaaagat tagggaaaaa 600

ggagaggctt aataactaag acacttggag cctaggccaa cgcgaa

646

<210> 629
<211> 617
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(617)
<223> n = A,T,C or G

<400> 629
gccccnccc cctcctnngg gcttatnngg acagaccac gtagtactct aaatcttctc 60
ctacgcgga caacggaccc tataccaatt cgaatcttgg acactccgac cgccggattc 120
tcttccccct tcggcttccc ctttctgtcg gtacccctcc ctagtcgtct cctacacctt 180
cgtaccgtcg atatatagtc gccgcggaact agcctattta ggtgtcctag actcgttatt 240
gatccactca ttagtctagt actatgcgtc acgtatctta gttgcctaag agggagatta 300
aatcctccac aagttccgac gaattcctgg actctcgtac tagcaaactt tcttatgagg 360
cttccttgta tatcttctgg atgtttctcg tgtcccggtc ctccgctact actagagctc 420
cttgccctat ctctagaagt agaggactct cgggttcggt ctccaaatct agcgctagag 480
ctatcgctac ccgctcgatt ccccagcgg aatcttgaaa cctgaggtag tacacaaacc 540
ctcncatct tcctcggtt gctccttctt ctcatcccc cttcccgctt tctcggaan 600
gaatctactt tancttc 617

<210> 630
<211> 644
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(644)
<223> n = A,T,C or G

<400> 630
cnntcggcnt gggttttntt ctgagnnncc ccccccccc ccccccaaa cttacacca 60
ccaaacactt tccgccccct acctaggaga cattagaagg gtttaggctt cggcgtag 120
taaagtccct tacctcgga gtagagaatt cggtatattaa attcagggtt agaggctcgc 180
tcgttagatt tatagtttag gtttagaatac ggaaaccttc gatcttcctt agaagggtaa 240
taagtgaggc cctaaatccg tctaaccaag gcgttaaggc cgtacctaa acctagtctt 300
atcttctatc aggcgacca atatatgtag gttctacttt cgtataggcc ttaaggaata 360
gttcggtagt tatcgaaggc actcctctct aggctaggct tttctcagtc ttagtactcc 420
gggaccgtcg tcgcanaaat atcgatggac ggtagggtatc tccgcgttac gcgtcgggct 480
agggatatac agcgaattat cggcgagagg cggctcgctan gaatcggtat caatatgntg 540
ttctttacc tacggatatc ggcagaaaac ataaaacct ctnaccangg ataagggtat 600
atcgacccc taaaataaca gtaacattta gantactagt accc 644

<210> 631
<211> 526
<212> DNA
<213> Homo sapien

<220>

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<221> misc_feature
<222> (1)...(526)
<223> n = A,T,C or G

<400> 631
ccntcggtt ggggtttttt ctgagcccc ccccccccc ccccccccc cccccccggc 60
cccatagccc caccggnccc acccaaattt taacaaaata aatntaccta tcgntcacct 120
atcccnegta tcgngtaggt cggtagccgt accgngatc ncnacgattn ttcgggtcgt 180
cncccttaan acggncccg agcncccgga anaaatacta cgagngactc taatntagca 240
anaccgccc tcnattanta gcatccttag tcttccaatg ncgnggattn ngaatccttn 300
naagttatcg ggtagaacgg gtcccgggtc cccgccctct ttncaattaa cgccgggtac 360
aaantcgggt tctaaattcc ncacgaattt ngncggcaac attcncgggn ccttattanc 420
cnthtccaac cccgatacnc nagctcgatc gggctttanc gaatccgggg tcnccccga 480
ngantccggg tcctttgagt ngctctagga cggttacgac ggagga 526

<210> 632
<211> 647
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(647)
<223> n = A,T,C or G

<400> 632
tttggngggc gggngctcat ttgggtggac tttttgggtc gtaggaacct ggtatgaggg 60
gtgttttagt tttcttcttc gtcgtctctg ggaggttcgg tttcgattga gattcggggt 120
cgtctttatc ttacgaggca ccctgatatt gttgcgcttt ggtttgggtg tggagagttt 180
tgtcctactc tagcgggtca tgccgatgat atgtagcctg cgtggcctga tagtgatgtt 240
gtgagcttga gaggggagtt gtgggtgttg cgggcggagt aggaggggtt ggagcaccgg 300
gattgggaga tatagaatca taagtgttag gtataggctg attgagcgag ttcgtggaat 360
tcgtgtggtc atcataatta gagtgaggat gggctctata tttcttagag gacgcacggt 420
cgtgattcgg ggtttgatgg gtgttcttct tgtgggcacg attagcttgt tcatgatggt 480
aaggaccata ctgtttcgaa tgaggattcg tgtcttcgga ttgttggtga tattgtggnc 540
tanactatth agtgaagcc ggaggtggtt tgccgtggtg gagtatccga nnttcattcg 600
ganggtatgc gtgcggagcg gtcctttagt acattccgga aaaatgg 647

<210> 633
<211> 630
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(630)
<223> n = A,T,C or G

<400> 633
tccttcgggt tgggtttttt tctgaccccc ccccccccc cccctcggga aggcctctag 60
gtctccaccc gtctctctaa tcctcaggaa ccgatccacc caaccaactt actaatgtcc 120
tacagtaaac acccgagaat ataaaccac acctaggcct ccaatcctac cagggaagca 180
agaagccgta gtctagcgta ttacgaaccc gagatagaga cggagatact tagttttatt 240
ctctcggaat aggaaagacg actggggagg gaatataggc tagcgcgggg ataggggcta 300

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tggcggatat	gggggcgggt	cgctctctta	ttcttctata	ccacgtcaat	aggaatgtag	360
atatacctag	atgttcccgt	agaaagagac	gttagaggtc	tccgaagcta	taaaggagag	420
gcgcgaagaa	acttcgtact	ctagctttat	ataggtagtc	gctctagtcc	cataagcgac	480
gagagatcta	ctagatttct	gtatcgccgt	cgtatgtatt	cgaaatagtc	ttcttcccct	540
tttcgatctc	ctctctatac	tacatggnga	ttatagtctt	aagatagtc	ggatattagg	600
atattagtta	tatgacgttc	gacggggacgg				630

<210> 634

<211> 647

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (647)

<223> n = A,T,C or G

<400> 634

ccntcggctt	gggttttttt	ctgaccccc	cccccccccc	cctccactaa	gancttaacc	60
caaccctata	gtttactcgt	ataggggaat	cgaggagaaa	taggaacgaa	gagcgggtga	120
taaagagaaa	gtactttcct	ttatatgtta	agagcttagc	gtaatgactt	tcgttatatg	180
gctagttagt	tttatccggc	gttatagggc	ttagtctcgg	ttatctcggg	tctaattccc	240
ttagtatgct	cgggagttta	acgaggtcac	gggatagcgc	gtaccctttc	taagggttctt	300
ggaaagctat	tcgttattta	tcgcgattct	cgaggtcgaa	aggatcaagg	atcttccctt	360
ttactaccct	agtcgggtta	gcggtcggtc	aaaactagt	tagtaccttt	acctcctcga	420
aagttatagt	cgaacaacg	tattagtcca	aattatagcg	gatagatcga	gacgggttctt	480
tctcgggttc	tcagccggta	atccctctat	ttgggggtct	tctccctctt	cccccttgct	540
ttccgcctta	gcttccaagg	ttcctcggaa	gcgaggggtt	ctacttaagt	cgntagcgtt	600
ccttataaac	cncctacagg	cagacccctt	tgtaaacggc	tcgggggt		647

<210> 635

<211> 645

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (645)

<223> n = A,T,C or G

<400> 635

ccttcggctt	gggttttttt	ctgagcccc	cccccccccc	cccgaaactc	gccttaccct	60
agatacccaa	agaatagttc	cactcaactt	cgtctaaagta	aaactctaga	acttccaaac	120
ataaaaagact	tcgcgcggtt	agctacacag	cctacgggaa	tctcacgaat	cccgattcaa	180
gtcccactct	cgaccacacc	ccggtatcgt	cgtttttccc	taccaatgtc	gaaaaataaa	240
ataaaaatcca	gtcaagcccc	acggtaagcg	ggggtagggc	taggcgaaga	ggcaggaacc	300
gttcgaggcc	gggggctttc	aaaatacaaa	acaactactt	aaagtttacc	ccttctaaag	360
tcgggggcaa	cgggttaaagc	acgcctctaa	agtactactc	gtttcgagaa	ggggtagtca	420
tctcccgcat	agagactctc	gcgtatatca	actcgcacgc	cttctagcat	tcgacgggtc	480
gcccgcggct	acatatcttg	cggattagct	ccgagggact	atagggttaa	ttagtctagt	540
aaattctctt	agaggatagt	cggggctcgt	gttaggcagt	acgaggggac	atggnctgcg	600
tcgtgctcta	ccttgacagc	atactcttat	aaacatcttt	ttcct		645

<210> 636

<211> 643
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(643)
 <223> n = A,T,C or G

<400> 636
 ccttcggctt gggttttttt ctgaccccc ccccccccc cctagcggaa aacaatcccc 60
 accgagattt tattaatcgt aaaactcgcc ttcggtagca agtcttcctc cttcccgtaa 120
 cctggctccc tcctagnngc ttacgaacg tccctcctct tcttacggct cggaagtggg 180
 tacggttaaa tccggaaggng gggctaacga atccaaggct aactcctctt anagtttggt 240
 gtccnncgt ttagtaagga tccgtggagg gcgagtattt gnccccggc ctttattnta 300
 tagttcccta gtacgataaa gntaccggct atcctattac agcggataaa agttatttan 360
 agggccgacg tcnccgctag acaggctaca gctagnngag gtaccgcctc cgactantcc 420
 gttgnttccg acaaggnagt ttcggttaac tccacaaact cctccgccga ctctanggtg 480
 gggacggcag ttccnncgtt tagtgtgcgt tatagagaag ggcatttgag ttggacgtta 540
 cnttttaaca taggttattc cgtttaggtt cttgcgggcc cgtgggggta gtncnccggc 600
 gcgttnntat cggcgatttt ccgcagtttc cgtttcgggn tnt 643

<210> 637
 <211> 631
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(631)
 <223> n = A,T,C or G

<400> 637
 gggttntctc atttgggtgg acttttttggg tcgtaggaac cggatatgnag gagtaggagt 60
 cgctgggaag actagaagtt agctacggac gattagtgtg attccactct taataacgag 120
 taatcgttta cgtcgggttg gtgtttcggg gttttggaga gtaagcgtag ttgtggagtt 180
 tcgcatatag gtccccttac ttcggcgatc tcgtcttctg tcggttaggt tattattggt 240
 catccttcgc attagtagta gggtttggtc gataaatcga tagctattct ttagaattcg 300
 tagtcggaga attcgtgtac gaagtccttt aagttcttta agttcgcgag taagacgtgt 360
 acggttattt tgtcgtcgac gtaggtgtcg tttacgggag tttcgtttta ggggtttacg 420
 tagaacgtta ttaagcacgg taatacgata gaggattacg cgacgtattc gtcttagaac 480
 gtcgattttt cgaaggcgca tttgttatcg aaggggagtc cttggagaat cgagatattc 540
 caagaatatt acggagatta cagatcggaa ggctcccag atcggacgta ttaccggtct 600
 cgcccgaac gagtaggtat cntccggata a 631

<210> 638
 <211> 606
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(606)
 <223> n = A,T,C or G

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<400> 638
ccccccccc ctcaaccatc nattccccac ctcaacgcga attacggttt cgaaagtcga      60
caataagtcc ggtcgcgtag aggggaatcag gggctggtan aaaggaccac gggcggaaaa      120
taccggctct cttccgggga ggcgcgctcg ggaaagggaa gagagcggtc tagttcgtag      180
gcaaacaggt cagaaaagtt aagggttaaag gtcggagggg agaggatagc tagtacgctt      240
agttcggggc tcgggcgcag ggccactttc ctcttttcgc ttcctttact ctgcttacga      300
gttcaggctc cggagttccg cgccggaggt cgtcgcgacg ctaggaatgg ggactcgctc      360
agtccccggt tatccttcgg gattctatgt tttcgcgat agacggagac cgggtagtag      420
ggttccgctg taccgccact cgtcgccttg atccggccc ctcgccttaa gggcgatgaa      480
agattagta ttagggctct acgggacgag gcatagggcg ggagaagggg ggaggggtcg      540
ggggtcgaag ggantaagaa atcgcantcg cgcggggctg gtagganccg aaatttttct      600
cnnctg

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<210> 639
<211> 592
<212> DNA
<213> Homo sapien

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<220>
<221> misc_feature
<222> (1)...(592)
<223> n = A,T,C or G

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<400> 639
tcctcggct tgggtttttt tctgagcccc cccccccccc cccccgggaa cgagaaaaca      60
atcccaccct accgcgggga gtgggttgna cgcttagttc tagaatcctc ggaatcgctc      120
tcggcgcttg gtagttccgg cgattccgag tatgcogaag tgtatcgctc cgtctagagg      180
ttgggtatctg tttatcgca tgacgctatt gactcggatg ctttcgaagt agggggatag      240
gcgcatagat acgcctccgc ggtgtcctct gaagtggcgc catccgtgga cgcagcgtag      300
acagctctgg tggacgataa cggcttctcg tactcctact ccggctatta tgtagagag      360
gacttgtttc tgaacggata taccattagc gaaggggtac cctccgctaa cgcaggcgtt      420
tctaacagtt cttccgggcg ctccgaattt agattgacgc ctccgcagca ttgtgggatc      480
ctcttcggtt agccctcttt ataggatttc tcctccgccc cgaaagangg ctggtcgtcc      540
ccggcangta tgtctagctc gaacgccttg ttactccttt gttttcgaaa na              592

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<210> 640
<211> 637
<212> DNA
<213> Homo sapien

```

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<220>
<221> misc_feature
<222> (1)...(637)
<223> n = A,T,C or G

```

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<400> 640
ctttgtggcg gtgngtgtct catttggtg gacttttttg gtcgtaggct tatccgggtn      60
gggctcccgga agtagcttag gatcgccggc tagttccggt cccgcccgtc gaaagcgcg      120
ttcggcgggc ggccccgctg tcgttcgcgg gctttaccct catagagtgc caggctctcg      180
ttcttacggg ttcgctcgcg atagatttta cggcgagagg tcggtatctt cgcgccttta      240
cgttcggctc gcatctacgc ctagttcaca ggtagtttat gcgccggagc gcgtgacgga      300
gaggttatac gggacgcgga agaaccgcct ccaaatagact agtacaggct cgttcgggcg      360
tagatctcct cgctcggtcg gcggttctta cttctagggc cgctctacgg ttttaaggcg      420

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tcgttagatc	ttagaaacta	tactcaagtt	tcagtcggaa	gaaaggaagt	agagagaagg	480
gtaaacgatt	acctccggtt	ctagcccttt	ttactcgc	aacgggagaa	cggggtccgg	540
ctctcagata	cgctcgcga	gacgtcgcga	ttcaacttta	acctccgcta	gggcatccgt	600
atacggttaa	cgcggtaaaa	gcgacctcgg	aaacctc			637

<210> 641

<211> 649

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(649)

<223> n = A,T,C or G

<400> 641

ctntgtggcg	gtggttgtct	cagtttgggt	ggatttttgg	gtcgtaggna	acctggtatg	60
aggtctagtt	tcttcaacga	ttcttggttc	agttacgcga	ccctatcctt	atcttacaat	120
gtcttctaca	tcaggttcat	caattaatat	atcaattaca	cattaacgac	gggtgtgacgc	180
aatatgagaa	agtatacatt	aaggttatta	tatattattc	gcttaaaaag	gttcctgaca	240
tgggacaact	tcaccaccca	ttctagaagc	ccccctcct	gtaggacccc	ctcgagttcc	300
ccattatcct	agttcagttt	tcatttttta	accaggaggg	tatcggtttt	taataggtac	360
tattttgtca	aacttttcag	aagctttatc	ttcaaata	cttgaccat	ctgtactagg	420
agcactaact	attcgagtct	attacagctc	aacagaaaat	aattgaaatt	aaacaaccta	480
agtatcgtec	accataaacc	catcgggctc	tcacccatt	tcttcataag	ttctagagca	540
tcttgagctc	tttctatta	cccttgatgg	tactcatggt	ctaatacccc	ccgcagttat	600
aggtccttat	ggatcctatg	ctaccaccgg	tctaatecct	tctatcacn		649

<210> 642

<211> 645

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(645)

<223> n = A,T,C or G

<400> 642

tccttcggct	tgggtttttt	ttcgtcgcgg	gttactatta	tcgattgtta	cttgtaaagg	60
cgatactccc	accgctcacg	atattagacc	tgtcctctc	gaagcgaacg	gcgataggtc	120
tactcggcgg	gcgaagacgg	cgaacgggta	ggaggagcca	tatgcaacc	taacggagat	180
tataagtact	gggaaaaata	ctagtattaa	ggtagcgggt	taagatagg	ggagagacac	240
tattcacgag	cataagcact	tagaaggctc	tctcgaggag	aggtaggcta	cggactacgt	300
tccttcttcc	tctagcctcg	agagggagta	tagatgattc	gcaaaagaga	atccctccta	360
tacgctggca	taactagacg	acgcgtcgtc	gggaaatctc	gccaacccta	ttgcgacctc	420
caaaaggaag	attgtcgttt	catagaacgc	taatactccg	gggtcttccg	aatcatagcc	480
gcatactcgt	aagaagacgg	taaaatcgcg	cgattctaac	aagattctgt	agacttaagg	540
ctaagcacta	gaagcgatct	cgattccgga	tcttaagatc	atactaatag	ttcggtcaca	600
ccagacgacg	attagccact	agaagcccta	ctccgtngaa	accgg		645

<210> 643

<211> 586

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(586)

<223> n = A,T,C or G

<400> 643

ctttgtggcg	gcggtgtctc	at ttgggttg	at ttttgggt	cgtaggaacc	tggtatgcag	60
ggtcgccccg	gaattaaaag	cgggatcccc	aaaacgnngn	ttcgcaagaa	gagaagaatc	120
atagcgatag	anc tttcata	gtacaaaggt	aactaagagg	aaaataatgc	agattcagaa	180
ctagttgcc	aattagaact	cgattaggcc	aaggatccga	gcctggcgct	atcacttcgg	240
gacttaagct	acggtagagc	agtcggtcct	gaagcatagc	tcccgtagga	cgtaggaaac	300
tagtccggca	cggaggacat	actctcgagt	ctcggaacgt	ctatttagaa	tataaacgca	360
ttaacctcag	aaggcgccga	cgcggttact	ctctagggaa	ctatttcatt	ccttccggag	420
ctccccatt	tttccaacac	atataccggc	aaaggaaaaat	cttntgtcct	cggctctaaag	480
agagggaaaa	aaaacgatat	ctaggttcgg	gtttatccat	ttaaaaaanat	ngacgcgact	540
actccctttc	aaagggagtt	tccccctagg	nagagttcaa	cngaag		586

<210> 644

<211> 646

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(646)

<223> n = A,T,C or G

<400> 644

ctttgtggcg	gtgggtgtct	catttgggtg	gcatttttgg	gtcgtaggaa	cctggatatng	60
agggctat tt	gacttgtttc	tcaa atccca	tggtatgggtg	gggtggcggtgc	gggggtggcgg	120
tcggttcggc	gggggtgggg	gtcgtcctcc	aaaggagttg	ctagagggct	tttagtggtt	180
ttagggcggg	aaggggttag	agcggagaga	cgtcgtcggtg	gaagcttctg	gcgagcgcgc	240
agaaggtagt	tagcgccggt	tcggaagatt	ctcagaattc	gagaagaggt	agtggggcgc	300
ggagagagag	tttctaagtc	taaacgtaga	ggtcgtccta	gtcggggcgg	gagtagcttt	360
taagctagag	gtcgaggtcc	tcgtttaggc	tccgggctct	tcgggcagta	tcctctttct	420
cgaggaacgg	agcgaccgac	gtcgtagccg	gaccgcgtcta	tccgtacggt	tagagatacg	480
ctcacctcca	cgggcgtata	tgcccgtata	cgtataaaacg	cgtaatatac	tcgcgcgtaa	540
aacacgtata	cactatatac	acgcacgtga	cggaccgtat	agcgttatac	gcgcgcgtat	600
attaattttac	acttatatac	gcgttaacac	gatatatcac	acnccg		646

<210> 645

<211> 654

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(654)

<223> n = A,T,C or G

<400> 645

ncntcggct	tggttttttt	tctgaccccc	cccccccccc	cccccggtcg	acaacgtgcc	60
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caccgttgcc atcccagcat agctggttcg ttctgtttta ttcttagtag tttagttcgc 120
ctatagtccc tcgtctatcg tctatcattt aaggaggcgg ggctcgctct ttagggcggg 180
tatcttaggt attcttctcg tttcggctgc cgtctcggag tctggtcctt ttgctttcct 240
ttcttggtcg aacttcgtgt ttgatcgctg tgtttctttg gggtcgcat acctaagggc 300
cacttcgcca acaaacaagt ttgtgtagtc gtttctatta gggttcgctg gccggcgctc 360
ttactggttg gcgattttta acgcgttttg ttttaatttg cttcctcccc tagggctcgc 420
tcggctctct ctctgttcgc tgcctcgcgc cggccttttg tgcggggata gctccggcta 480
ttancgtgcc gtgtccgtgt ggnttttgtc caatgtgaag gcctaggggt gcgggcttct 540
ttggccatgg nttccctct tgtgancctt aggggtaacg antcgttaatt naaggtcggg 600
ggttggnata cgttntangg gangcctgng tccgntattc cttgttttgg cctn 654

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<210> 646

<211> 645

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(645)

<223> n = A,T,C or G

<400> 646

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tccttcggct tgggtttttt tctgagcccc cccccccccc ccccccacgcc aagtacacag 60
accacacaaa aacaacgtca acacaacttc ggggtatacgg accttaagag agaccccgtta 120
gtagacccta ccacagccat ccaatagtc aacaacaagg gcgcacccaa tccatccata 180
gagctatcaa acaacggagg ggaaaggaaa gagcagggtc aacttagcag agatcgaagt 240
cggcactaat tcctttcaag tactcgctcg gctttagtct cggggtaaaag tccgctctca 300
aagggccaac gaggttttaa agcgaccccc gtatcgagtc ttcttcgtat tcattaaggc 360
gttaaaggta cgagacctag aagagagtag aattagccca ccaaatacgcc taaaccggca 420
aaaacgacca aaagtcaaa acccttacia atatcacctt aaaacgcaa ccccaaaaac 480
gcgatcagta acgcacgtac ctttcccaag cttttctttc tttcactctc caaaacaaac 540
ccgaatatct agcgcaaaaa atatccgagg gagaattaga agctattacc cgaaaaaaa 600
ncgganangg antaaatngt ggggaatana cgtttggttt ttctg 645

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<210> 647

<211> 753

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(753)

<223> n = A,T,C or G

<400> 647

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accttacctg gtaccgggccc cccctcgag tttttttttt tccaaataca actcagattg 60
tatacgaaaa gctgataata cattgacttt tgctgtttta atcccttgag cttttgataa 120
tgattttttt tgtgttaaca attgtagtat ataaaatcgg attcaccatc cttctgatgc 180
catattgatt agtttgattt tatggtgatg ggatcattgt gtgttaactg tattaagaag 240
aaatggattt gattgacttt gcatccattt ttatctgtgt tactttcatg ttttatataa 300
aagcatttct ggaccagaat aagttaagt gtataatttg ctttttacac gtttatataa 360
ttgaagttag caatgtggca aaatctctaa tggaaataaa atgcttcaga atgatgacat 420
aaatctgagc tatttcttgc ctggagaaca agtggtattc ataataattt aatagcttct 480
gaggtgtttt gttcatgtga tgaaggctta tccaccttgt atcaattcat gggctctgct 540

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ttgtttaatg tagtcaggtt gttaatacna gacttaagag tcatcctact gtgataagtg      600
gtgagtgaag attacatgtc ttangaaaat tatactggga atatctctga cattaatggg      660
tttaaatggt ttaaggctag gggatgatgc aatgganaan atncttccaa angtttctgg      720
ttgtttatat ttgnngaagn catnaagana ccg                                     753

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<210> 648
<211> 383
<212> DNA
<213> Homo sapien

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<220>
<221> misc_feature
<222> (1)...(383)
<223> n = A,T,C or G

```

```

<400> 648
gatatcccgg ggaaatgcgg aggcctttng gcttacgtgt ttaccgcgta gggcaaagcc      60
ttgncaaatt cccggccagc ggagcggcga ggggtggggac tcacgggaag ttaaacagcc      120
tcgtcggcgt cctcgaggct ccaaaaccag gctctaggcg gggacgactg cagccgttat      180
ggaggccacc gcggctacgg ccgcggctga ggccctccca ggtggagcgg tggcctggag      240
gggaatcttg atcctgggcc agccacctgt caagaggagg cggagcgtca tgcctctgga      300
agactggatg aatattctcc aggagcctga cgaaggcgaa gaagtctttg cagaggaaat      360
tgaatgctgt ctgatgctac aat                                     383

```

```

<210> 649
<211> 349
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(349)
<223> n = A,T,C or G

```

```

<400> 649
cgattgtnta cnagtcttag agtaagctta agntcgntac cgagctcgga tccactagtc      60
cagtgtggtg ggaattccat tgtgttggtg cactagtaaa tggatttagc tagacanagg      120
anatttaccb tattccattt agcacagtga gganaggcta nacagctagg atgcaataaa      180
aaaaatttta atgagaaatg tgtgtggttag attaattcta ttaatctcaa gttatagatt      240
aaaaaattta agtaccncat aaatgccatt tgcctttgct aangntacat ttttatgaan      300
aangacntg catacnaat ganatactgg actttnngna cttgangga                    349

```

```

<210> 650
<211> 306
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(306)
<223> n = A,T,C or G

```

```

<400> 650
cattgtgttg ggagcatcct tccatcagct cccatgagaa attctctgtt gggtttaagc      60

```

aatccccaaa	tatatcatat	tgacatgaat	atatcatctc	ctcaatgtcc	agcattagca	120
gacaagatga	gtgctgaaga	tgatataact	cctacctctt	atgtaggcta	gaggtaaagt	180
ctggctctgc	tgactgtggg	gacataccga	aaaggaatgt	gggttaatat	cagangacct	240
ccctgcagat	ccganantca	gggnctggac	tttctgggan	aggaagcna	aagttatntc	300
tgaacc						306

<210> 651

<211> 769

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(769)

<223> n = A,T,C or G

<400> 651

cattgtgttg	ggcaggggtca	tttctaaggc	atgggctgga	agcttttatt	taaaacttta	60
catgtcttag	aagcactctg	gttggttgcta	ggcagacaat	tttacatctc	ttgctatacc	120
agttgcatga	agttcatcat	gcataattggc	tgtggaaaac	cttaacagca	tcatgtcata	180
aggtttcagt	aaggtttaaa	tgaaatcatg	tattaagcac	ttagtatagt	gcaccttaaa	240
tgttagcttc	aaaacaatga	caacctaaact	aatggtgaaa	gaagcttggtg	tttgtaaatt	300
atgtcttatt	gaaagatgtc	atcaaatoct	gttattttcta	atcccttaaa	gtctctcaat	360
gtattttcttt	ttgccatatc	caatgacagg	accttagttt	aagccagtgg	ttctctcaac	420
ttctaatacca	gagataacctg	ggtgtcccca	agaccttttc	agagcatcct	tgatgtcaaa	480
accattttca	taataatatt	aaaatattat	ttgtctcattg	tactcttatt	ctctcccaaa	540
tattcagcga	gttttccaga	agctatataa	catgtggtaa	catcttatca	ctctgacgat	600
taatagaata	tgngnttttg	gattcttgng	tttaaaattt	tctcactttg	gggttctaatt	660
atggnnacga	ttaatagata	tggnctccat	gaccagangg	ctttaagca	ntcaataatt	720
tttaagagac	taagnactat	cctttaaaga	tnngnaactc	catcttaatt		769

<210> 652

<211> 267

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(267)

<223> n = A,T,C or G

<400> 652

nnangccctt	taaccattgn	ggcctccaag	cnntggcggc	cgtcttacia	ctagnngatc	60
cgnactcta	gnanaangat	tggtcttnt	gggntgggcc	ggncgggctg	gggcgttaag	120
cggggctggg	cgcgcgcgn	ggttgnacna	ggcgccgcgc	ccncacacn	cccggagcac	180
cctcnttgc	gcctncccc	gctcaccocg	cgcgcgcgn	tecgttttt	ccncaccan	240
agcnctnttt	atctntgtct	cctccgg				267

<210> 653

<211> 501

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature
 <222> (1)...(501)
 <223> n = A,T,C or G

<400> 653
 ccnttnacc cattgctgga ctccaccgcg gtggcgggcg ctctanaact agtgggatcc 60
 ttncnatgag atngcgcgag gaggacnnat ttgctatnct ggatggggct gantcntnta 120
 gctnctctag cancagatgg gttatcgagg aagatgactc caangggcta nantcctatg 180
 cncatcctaa aanncanctg ctgtnttcag agtacgcgac acatcatcnc tnatgcattg 240
 ntgancaaga cgggcangtg cttatcctca gcgangatgc ccttaaccan gagctcgaat 300
 ggacntatca cnttanaggt acanntnccg caccacacac cngcttgcn cctgacgctg 360
 gactggatcn cttaggccac caatnccccg tttnccacat ncctgggacn ctananatac 420
 tcganggggg gcccgggtanc caattcgccc taatactgag ccttgntacg nacgctnact 480
 ngngtccta ttanaacggt g 501

<210> 654
 <211> 710
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(710)
 <223> n = A,T,C or G

<400> 654
 gcgnctttan cncatgctgg gctccacgcg gtggcgggcg ctctacacta gtggatccca 60
 aactgagtc caccacagna aaactcanca ccaggcagac cccacaactg cagaatccag 120
 gctgcaattc acagactaat cntctagacc cacctcagta ccagatggta ccacacagct 180
 caaggnttta ggtttgctg gtanactcaa tctctatctt tcaccactgc cagcctgact 240
 tcagagatcc tnggctctgg acagtccctca gtggcaggca actctcagga gcctcaggnt 300
 tttggcacat ccagnacca gccagctgcc acaggccctg accttntanc aactgccc 360
 atgtattcca gacttctanc ataccacagt gccatgctga ttgcatctat agangctcag 420
 gtgcncctca aanctgtgcc tgctgcagna ngccccacgt ctctggcatg ccccaatgcc 480
 atngtggnna acanttgact tctgggcatg ntgggaattcc ctaccactga ncctgaccat 540
 agngggganc ccattttttt cgaggggggg gcccggcccc caattccncc ntatagnag 600
 ncgtanttac gcgcnnctta ctnggcngt ngtttaacaa cgtcnntgan ctggggaaaa 660
 cccctggnng cnaccctaat taaacngcnt tgcannacat cccctttctg 710

<210> 655
 <211> 202
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(202)
 <223> n = A,T,C or G

<400> 655
 ccccttttnc ctttcancnc ccccgttttg gngcgcgcn acacctactn catccaccca 60
 cantegacca ccgagcttt tttccgateg cancatcnat gnggattttt tctntgcntg 120
 ctngcctgc acctttgnta ggtcaagcct ggcccatctt cgacaacttc ctcacacca 180
 acgatgaggc atactctgac ga 202

<210> 656
 <211> 308
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(308)
 <223> n = A,T,C or G

```
<400> 656
gctgntgaaa gaccacaccg aaaaactctn ctttccgact tccacatgat gatcngcatg      60
tggtggtgag agacttatca tgacgacatc gcttccnacc atcgcanccn ctgcccgaagc      120
ccattcatgg aggcctgggn anttctgtga ntgacntnga cncctanacnc tncactgtn      180
tgctatccag acttgnttng aatatnttat tggcnaaaana canttnccgga atgctgtgnt      240
tgnnccattga angatctgat cactatgaga ggggtgaggac nncctgctng ctggcantnt      300
ntaaccn                                           308
```

<210> 657
 <211> 696
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(696)
 <223> n = A,T,C or G

```
<400> 657
accnttttcca caatnctggn ctccccgcgg tggcgccgcg gtcgaccagc aacctcagct      60
gtgggtcttg ttacagtaat gagttactgt aaggaaagtg tgacatttcg agcaatttga      120
tttgtttaaa aactagagca gtttcagggt tttccttgta aatctgtctt atgtgtcttc      180
aatgtttctt cttgaggagt agagaaagga attgttagga atgatgcata aaccatggct      240
tattttatct cgctgccacc cataatcaga gcagattctt gggactatga ccctcatgga      300
gacatgacaa ttgtgtgtgt ggtgggtggg agaaaagagc tgggaatttt tagggtctag      360
agggtcctaat caggactatt ttatggagct ctgctcacca actttaagtg agcaccaggg      420
gtgngaaagc gaatcttggg ntcaaaaana caatggnaag gggtaagttg gtatnctgaa      480
ctggccactt cggactctta tttaactggg tattctcant taaggaggcn ngggtggtct      540
tggccttgtna aggaaagcct gtgcaatgga atgactttta aaccccccat taaaaaaaaa      600
angntataaa tcttgggtct taanaangaa gcctgggttc tnttanccca ttttnccccc      660
gggaaggnaa atnttcttag gnaanggaag ggaagg                                           696
```

<210> 658
 <211> 698
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(698)
 <223> n = A,T,C or G

<400> 658

```

ctggactccc cgcggtggcg gccgctctag aactagtgga tccgtgttgg ctcaattctc      60
aaggctgttg ctgtgcggcc tgttccccac acgtgctgct cagctcaggc aagcaccgag      120
cttgtgttgt ttcattgctca gcgtggaggc ccctcctcca ggtcgctgct ctgtgggggt      180
cccatacact caggctccta ggaggagtcc atttagaaag ccagggtttt tctcagagtc      240
ttagttcctt gtgctgtcat ccatttcaca cgacttgggc cctgctcggg gcaacacagc      300
aagagaaaag acaggggaaaa taagagaggg accttgcaca cacacgctct ggaccacaga      360
gccctgtgcc cagctcctct gtcaatacag gtggaatctc gtgcaggatc gcaggggtct      420
gtgatgccac caaagagcag gccgggacag ggtaggaga gaaaggagag ggaagtgggg      480
gtttctccta cgcactctta tttgcagagg gaaaggcggg tttgtattgg ggttgtcggg      540
ctttgcaccc acngcacagt tgtgagacac ccccatcctn agatcaaagc cccacataca      600
gcttggggaa aaacaaaacn aaacaaaaca aaaacagtaa acctccatgc canttgttgg      660
gnaagttttn aatttncttc ccnaccan cttgcttc      698

```

<210> 659

<211> 750

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(750)

<223> n = A,T,C or G

<400> 659

```

ncaantcggg ctccaccgcg gtggcgggcg ctctagacta gtggatcctc ctcatgggcc      60
tggatatctc tgaacatatg atgaacattg cttatgaaaa attatttgta ngaaaattgt      120
gaggcctaag aatgntattt tcttttagtg atggtctttg tttgcttctg taagnactt      180
gtgggcactc gtaagcttgg atctctttta tctaatacca gntttgagat tttcttggcc      240
ccatagatga attaaaactg gcgtacttct tgtttacaag anggataagt ctctagggt      300
aagtcttttg ggtcccaag tcaaaaagat gagggattta ccagttctct aaccttggt      360
gccccagact ccaaaacttg ccttctagtc ccaagaggct atcaaaaagc aaaggccatc      420
ttccaccttc ttttccanaa cagcacacat tccagacagt acttgaaagc aggaacctcc      480
ttatccctta aaaacctctt ggaancatct tccctctctt gcttctacta tgcttgcccc      540
acctancatt cncntttttc tggaaaccgg aaaaancttn tgacttnngt tggctacatt      600
cagcttggcc ccctacaatn tggtttccat ctgccctaan gaaattttta agggcacttt      660
ttttntggcc cctgactttc nnttttagg gctttcccc angctttgcc cttttgggt      720
aaggggttat tttccttccc cttttggaag      750

```

<210> 660

<211> 849

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(849)

<223> n = A,T,C or G

<400> 660

```

tcggatccac tagtccagtg tgggtggaatt cgcgggccgc gtcgacgggc agtagtggt      60
tgcntntcta aatgttataa ttatttcaga attactctgc cagaaagtta tgatcataca      120
tagaagagtt tgtagctaac tttgaaagta gtggaaagtg gttttcatgt attgtttggg      180
ttaatttaat tttgattata tttgggtttt agttcaggta atttttttgt tgaaaacttc      240
aaatgacaat ttcttcatgg ttactaaaga tcaactcatgt ggagtagttt cagatttttt      300

```

```

tctgaataca tgtattactt ttagagatgt aaagatgtga aattactaag agagaaaccc 360
atgtgatttg tttagtggat caaaagtcgg tagctccttt gatcctaagt gccactgata 420
gttaaataga tactgaagct atgggcaggc tggattgata agaaaaaagg agacagagaa 480
atgggaaatt gggaaagaac tgtgcaaata ggaaaaggag agagcaacag aacagaatta 540
gtaccacagt gccgaagtgc caccctcaggc acttccatct cccatctcct gaagaattca 600
gtaacagttt gcaaattggc aacacaatca tttagtgate ctgggttgata ttttcaatac 660
tttctgggga tttcttggct ggnttcaaaa gatgatgctg atagttttat tgcccctgaa 720
ggattcttga agnttancat aatttattgg tcagtaaaat atttgaataa aagngganga 780
aggaaaatct ggcntcttat tttgggatnt cngcnggggg aangaggata taattnacc 840
cggccttg 849

```

<210> 661

<211> 653

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(653)

<223> n = A,T,C or G

<400> 661

```

aacttaagct tggtaaccgag ctccggatccc tagtccagtg tgggtggaatt cgcgggccgcg 60
tcgacctcca ttcgtttctt gtccctttttt ttcatttttt ctcattgttct attcacttta 120
ggttttctaag ataaatatta taaaataatt tttacttata aattattcac tgataccctg 180
tctttaacat gtgaaatgaa ttcaaaagga atcttaatga gaaataatat actcatgatg 240
tttaatagat ttgatttcga aataataagc cctctgaagt cctaagttaa aaataaagca 300
acttgtttga taatttttca tcaagaatgt atctgagtct ctgagtaatt attagtagga 360
atattccatt atcacaatta cacagtataa gctatttagt ctaactttac caaaaaaggg 420
agctacttca acactgtgtg agacttttaa tgggtttgca ttgggtatgc actattagca 480
agataaccta ttttacagca gtgtttntta acctttocca tttatttgaa aggcagctaa 540
gatatagtag ttaatntaan gggctgatgc atttatatta catgtagana atgggagata 600
cnaaaggag nggggggana tnttttgnat tcnnaagctt cnttgncaat taa 653

```

<210> 662

<211> 646

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(646)

<223> n = A,T,C or G

<400> 662

```

aaacttaagc ttggtaccgc agctcggatc cctagtcag tgtggtggaa ttgcgcccgcg 60
cgctcgacca gggacaggca gccagnctg gggtcaccag ggtcccctct tgggccctcc 120
aanagcaaca gtactggcaa cagctgggat ttgctgagca cagactctgc agcaggctcg 180
gttgagctct ctgtgcctgt tccttcatac catcctcacg cccatccatg agatgggtcc 240
agctgttttc agatgagaaa atggcacagg aagctggtaa gtgacagtca gaaatgaatg 300
ctggcagctt antccttgga cccaccgcag tgcaggacct tgcacaacag ggatcacctc 360
tgtccgccac ctgttcatga ggccaccag ggtttgtgtg gtcatttgtc tcctttcatc 420
tgcttgccct caaccagctg ggtcattagg gctggggaac ccagacccca cacagtcctt 480
ctcccagang ccagacacan nctncgccac agnaaggact tcagtcctccg aancaaatgt 540

```

```

ncctgggcgt anaaactgna gggnccecaa tccctgggtgg ggtactgctt tgcactggng      600
gaattcaccc ctcattgnna acctttccct nttncaccc ctaaac                        646

```

```

<210> 663
<211> 650
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(650)
<223> n = A,T,C or G

```

```

<400> 663
aacttaagct tggtagccga gctcggatcc ctagtccagt gtggtggaat tcgcggccgc      60
gtcgacgtcg acgcggcgng ccgtttcgac gcagttgata catattatta tatactacat      120
nggttttcta gaattaaaaa attaatgtgt agtgccagcc ctagatgtaa gttacatata      180
tcaactctat ccaattttgt cagccataaa acttaccttt ttcacatact tctaactcta      240
acaatgtgag aaatgtagat cattgcaatt ataccacaaa ggcagatggc tacatgcaga      300
atggatagca gaatctagct acttacgcta gccacatggg agacgttttt tcctttgttt      360
ttgcaaaatt gcaatataag ttgcatatcg ttagagttaa aagatgtaaa gaacccatag      420
aagccagtga tgaaggacat ttatatatttc acctttacaa angaccttaa aattgcctat      480
gtggagcaga aactggagga gggcnaancc atcngtaaaa aaaattttgn tnctatttgg      540
atttgggcac cattattacc tccccaggtn cctttttgnt ttaacctttc ttttaaaaaa      600
aataattcnt aattttttggg caaaaaaaaa caaggttttt atttaaattt                650

```

```

<210> 664
<211> 678
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(678)
<223> n = A,T,C or G

```

```

<400> 664
taaaaaatcta gactacacta ggaaattatt ttantatcag aagaatatca ggggtgtagt      60
actcatcana gctaaatgag agcgctttta aaatgttagt ttgtcttcg ccatttctac      120
agaaagctgc aatttccagg tttcaacctt ataggtgata ttttaagaaaa aaaaaaagca      180
atcgcaaata gccccactgc ttttacaatt cattttttct cttctaggta tagcctgtca      240
ggtggcctaa tgtaattttt gacatctcta ggaattttta tagaaccaga aatgggtgcc      300
agagatatgc ctgcactaat cttaagtggg gatttatgta tttctcaagc aagtgattaa      360
agcaaaacta ggcacgattg aaatcaanat cttttaggca agaaagtcac gatgagtttt      420
anaattatth taggactctg tggcttttct ttcatagaaa tagaaaaaaa aaattgtata      480
aaaaccacaa aaggtcctga atagcccaaa gcaacactga acaaaaangaa caaagcagga      540
agcaacacac taccggaatt caattatact accaaggtgt antaaccaaa acagcattct      600
attgggcata aaatagacca aagaccagtg ggaaacagaa taaagaancc caaaataaat      660
cctatattta cngcccncc                                     678

```

```

<210> 665
<211> 694
<212> DNA
<213> Homo sapien

```

<220>
 <221> misc_feature
 <222> (1)...(694)
 <223> n = A,T,C or G

<400> 665
 cttttcaaatt cattttttnct cttctaggta tancctgtca ggtggcctaa tgtaattttt 60
 gacatctcta ngaatttttaa tagaaccaga aatgggtgcc agagatatgc ctgcactaat 120
 cttaagtggg gatttatgta tttctcaagc aagtgattaa agcaaaacta ggcacgattg 180
 aaatcaagat cttttaggca anaaagtcac gatgagtttt agaattattt taggactctg 240
 tggctttctc ttcataaaaa tagaaaaaaa aattgtataa aaccacaaaa ggtcctgaat 300
 agccaaagca acactganca aaaagaacan agcaggggaag caacacacta ccngaattca 360
 aattatacta ccagggtgta gtaaccacaaa cagcattcta ttggcataaa atagacacca 420
 agaccaatgg ancagaataa agaaccacac aaataaatcc atatatntac cgccanctga 480
 ttatcaataa cnaacaccaa gaacatatnt taagggaent nctattcaat aantagtgcct 540
 ggnaaaaaact gggaaatcca tatgcagaaa naatgaaact agacccttat ccctcaccat 600
 acgcaaannt caacttcgga atgggattac aaaacttaag acattccaac ccaagaaact 660
 atnaaancta ctattaagaa aacagatcnc nccc 694

<210> 666
 <211> 705
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(705)
 <223> n = A,T,C or G

<400> 666
 tttaaaaaatt tagatacact angaaaatta ttttagtatac agaagaatat caggggggtgt 60
 agtactcatc agagctaaat gagagcgctt taaaaatggt agtttgtctt ccgccatttc 120
 tacagaaagc tgcaatttca ggttttcaac ctaatagggtg atatttaaga aaaaaaaaaa 180
 gcaatcgcaa atagccccac tgcttttaca aatcattttt tctcttctag gtatagcctg 240
 tcagggtggc taatgtaatt tttgacatct ctaggaattt taatagaacc agaaatgggt 300
 gccagagata tgcctgcact aatcttaagt ggggatttat gtatttctca agcaagtgat 360
 taaagcaaaa ctaggcacga ttgaaatcaa gatcttttag gcaagaaagt catgatgagt 420
 tttanaatta ttttaggact ctgtggcttt ctcttcatag aaatagaaaa aaaaattgta 480
 taaaaccaca aaaggtcctg aatagcccaa gcaacactga acaaaaagaa caaagcagga 540
 agcaacacac taccagaatt caaattatac taccaagggtg tagtaaccaa aacagcattc 600
 tattgggcnt aaaatagacc naagaccaat ggaacagaat aaagaaccca aaataaatcc 660
 atatttttac agccagctna ttatcaataa aaacnccaag aacnt 705

<210> 667
 <211> 817
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(817)
 <223> n = A,T,C or G

```

<400> 667
nnangacttt tgtggtnnta tacaattntt ttttctatth ctatgaagag aaagccacag      60
agtcctaaaa taattctaaa actcatcatg actttcttgc ctaaaagatc ttgatttcaa      120
tcgtgcctag ttttgcttta atcacttgct tgagaaatac ataaatcccc acttaagatt      180
agtcgaggca tatctctggc acccatttct ggttctatta aaattcctag agatgtcaaa      240
aattacatta ggccacctga caggctatac ctagaagaga aaaaatgatt tgtaaaagca      300
gtggggctat ttgcgattgc tttttttttt tcttaaatat cacctattag gttgaaaacc      360
tgaaattgca gctttctgta gaaatggcgg aagacaaact aacattttta aagcgtcttc      420
athtagctct gatgagtact acaccctga tattcttctg atactaaaat aattttccta      480
gtgtagtcta aactttttta aaaagacatg taatccgcgg agtttgtaac tcaaaacgag      540
tgcactaggg aggtatcgca agcgtttct ggattaaatt cccagctagc ttgcttgctt      600
agcaggggcy ggnaaanaag acatctgcag cctagggag aaacctttc gcattgttct      660
tacgtgttta cgttatttta tttcctanaa caaggcngaa ttgggactcg aatggttcag      720
ttggggtggy ggatcccctg gtncataaaa ngtcanaaag anggtacagg cggaacacca      780
agggtcgtcc tgcatttana ctcggaattt tggtgcc                                817

```

<210> 668

<211> 826

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(826)

<223> n = A,T,C or G

```

<400> 668
cgggggggnnt tacgtctctc tggacgcttt tattgtacca gggcgatccc agcccaactg      60
taccattcga gtccctactc ctgccttgct ctagggaaat aaaataacgt aaacacgtaa      120
gaacaatgcy aaagcggtttt cttccctagg ctgcagattg tcttcttcac cgcccctgct      180
tagctagcta gctagctggg aatttaatcc agaaacggct tgcgatacct cctagatgca      240
ctcgttttga gttacaaact ccgcggatta catgtctttt taaaaaagtt tagactacac      300
tagggaaaat tatttttagta tcagaagaat atcagggggt gtagtactca tcagagctna      360
atgagagcgc tttaaaaatg ttagtttgct ttcgccatt tctacagaaa gctgcaattt      420
caggttttca ncctaatagg tgatatntaa gaaaaaaaaa acaatcgcan atagcccact      480
gcttttacia atcatttttc tcttctaggt atagcctgtc aggtggccta atgtattttt      540
gacatctcta ggaattttta tagaccagaa atgggtgcc gagatatgcc tgcactaatc      600
ttaagtgggy atttatgtat ttctcaanca agtgattaaa gcaaaactag gcacgaatga      660
aatcaagatc tttaggccag aaatcatgaa nanttttana attattttan gaatctgtgg      720
cttctcttct taaaatngaa aaaaaaattg tttaaacca naaggtctga ataccaagc      780
ncctgaacn anagaacaan gccggagcac cccctcccaa atcccc                                826

```

<210> 669

<211> 547

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(547)

<223> n = A,T,C or G

<400> 669

```

cattgtgttg gggaaaaaat gatttgata agcagtgggy ctatttgca ttgctttttt      60

```

```

tttttcttaa atatcaccta ttaggttgaa aacctgaaat tgcagctttc tgtagaaatg      120
gcggaagaca aactaacatt tttaaagcgc tctcatttag ctctgatgag tactacaccc      180
ctnatattct tctgatacta aaataatttt cctagtgtag tctaaacttt tttaaaaaga      240
catgtaatcc gcggagtttag taactcaaaa cgagtgcac tnggaagtat cgcagccggt      300
nctggatnaa attcccagct tgctngcttg ctntagccggg gggcggtnaa aaaaacatct      360
gcagcccnng ggnaaaaacc ttgcatttgt tcttacgtgt ttacgttatt ttatttcctt      420
nnagcaaggc ngggantttg ggactcgaaa tggtagagtt gggctgggga tcgcccttgt      480
tacataaaag ncgtccagaa gagggacggt tacaggcnng ganctccaaa ggtcagtcct      540
tgccatt
547

```

<210> 670

<211> 232

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(232)

<223> n = A,T,C or G

<400> 670

```

cgaactatct agactaccta ggaaaattat tttagtatca gaagaatata aggggtgtag      60
tactcatcag agctaaatga gagcgcttta aaaatgttag tttgtcttcc gccatttcta      120
cagaaagctg caatttcagg ttttcaacct aataggtgat atttaanaaa aaaaaaagc      180
aatcgcaaat agccccactg cttttacaaa tcattttttc cccaacacaa tg              232

```

<210> 671

<211> 214

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(214)

<223> n = A,T,C or G

<400> 671

```

ctcccccttc ntccttcgct actncncatt ttcnnaaatt tntttcgcnt atngggaaaa      60
acaccacat tnttcancct gcacagaaca ngngnggggtg tgtaaaatga agggcttccn      120
cnctttctct tattnaanaa cactnaaana ggganggggtg aaaacccgcg ngatntctac      180
nctatecgcg gcgcttttgg ngttggctag aaga              214

```

<210> 672

<211> 328

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(328)

<223> n = A,T,C or G

<400> 672

```

ngancagcgg ngtttaaacg ggcctctaga ctcgaggaga cnctgttgg atggtggatc      60

```



```

acanntcgnt actactatac aggacagagt atcggganct cttggntggt ggngcctgcc 120
aaccactgct nctgttaact gcgtatctga agggactcgg actggcttca gaagaactac 180
cggctcgaat gnaccatgga tgattcncnc tagttgaaaa aaaactcagg cacatgtatt 240
gccactgatg actagecgcca gactnctctc ggctctntaa cgagcccaca tgnctgtgtg 300
ncncccggtg tgntccaga agagggttc 328

```

```

<210> 673
<211> 223
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1) ... (223)
<223> n = A,T,C or G

```

```

<400> 673
gggggcaaaag ctggctagcg tttaaactta agcttggtac cgagctcgga tcccnagac 60
attgtgcatg aaaatgcaaa ttgagtgtgg tctatantgc catctcacc tntgncngc 120
tcaaaacaac ngctttctgc tgcaatgggt agggctcctn acncacggtc gcnnacggag 180
gccnnccttat cctctcgggt nnggatccct ngaagcatnt tct 223

```

```

<210> 674
<211> 256
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1) ... (256)
<223> n = A,T,C or G

```

```

<400> 674
ngggggtcnt ngatgagcgc gcgtaatacn atcactntcn ggcgngntgg gtaccgggcc 60
ccccctnaa gcggccgccc ttttttntt ttttttcatt acatgataa ntcttnttc 120
taaacagacc acaccactan agttcctttt ctttngtacg gaattgagtt aaagtagagn 180
atacaatgca gggcttcnnc tctatttcac attccaggnt ggttcngnat ggatcggccc 240
tgctctccg atgggt 256

```

```

<210> 675
<211> 439
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1) ... (439)
<223> n = A,T,C or G

```

```

<400> 675
nnactagtcc agtgtggtgg aattccattg tgttgggctt gtatggggtt tttgtctag 60
ttntttggga aatgttngtg ttactatntt ttggatatna tatatgatat gtatggccct 120
tctatgggct cctcanacng aactcaacca tttccacaa aaccnattcc tcctttccct 180
tcatgactga gtgggtgttg tactatccng gaaactggga cattgtcctt cacatctntc 240

```

```

ccttanctgc ctngtccnat tgatgtcttt gagctntgan atgtctttgt taactntctc 300
ctnctntctgt actgccggca naattaagca ccatntgtca caaaaagtat tgcgttacct 360
tcacgnatct gttngttnc atncttgctg cttctccngn ggaaaatagg ctnttctggc 420
aaccgaacng aanaaatac 439

```

<210> 676

<211> 587

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(587)

<223> n = A,T,C or G

<400> 676

```

ngngggcctn attaagcgcg cgtaatacna ctcactntgg ggccaattgg gtaccgggnc 60
cccccaagt tnatntgccn aacctctctt ttggaataac aaaaggttta acacatatgt 120
cctcataggg acgcgctttc acacnttctt gaengcttca tanacntcat tntctattct 180
cctcagnaca agttnaggcn gaagggtgagg canacnttat aatttccatt tcacaaatnc 240
ggaaagttag gctcaaaggg nttaaaaaat aacctgatac aantcataga gccggtnctc 300
ggaanaagca ggagcaaagt ccaggcatcc tgatccaagc tnggtccact gccttccact 360
ctggagaggg ttcactctccg acaaaggaag ggacntgagt ggctgganaa tctcatggga 420
taaagacctc agnatcttcat gctcctggaa atcccatggg ttgaacaaca ggtntttggc 480
ccgtggttct ntccctttgn ccatctttta accttggggg aaatgatggc ntctntnagc 540
nttttttttn aaagagatng aaattgaatg attattingt cattggg 587

```

<210> 677

<211> 444

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(444)

<223> n = A,T,C or G

<400> 677

```

gtggggcatn attaagcgcg cgtaatacga ctcactatag gggcgaantg ggtaccgggc 60
ccccctcgaa gcggccgccc tttttttttt tttttactgt ccaaactntc tatngatnta 120
gttgaactgt ncaacgattt catgaaatcc tatacacana gccttcaggc ccagagagta 180
aaacaaatth aaatttnttc accanattgn agcagncana agcatccnat natatccgac 240
tacaatgaat natatgctna nggtanctna tttaccact ntggggtctt tanggtctgt 300
cacaaactat tttcgtaaac atcnntttta anttnggtga atggacctaa tnccagataa 360
ntctatttna tntaccctag catncctgtg gctnactttt cgggctgtgt tggcntactt 420
ttaggagaaa attggtataa atnn 444

```

<210> 678

<211> 670

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(670)

<223> n = A,T,C or G

<400> 678

actagtccag	tgtggtggaa	ttccattgtg	ttgggagcag	tttaaaaaaa	aaaaagacna	60
aatatacnac	tcttgatnaa	acataaaggt	acagtggctt	atgaggaana	gaaaaggtag	120
ctnaggatgc	aaaantacct	accacatggg	aaccgttngt	ccacactcat	tccnnanaaa	180
accgagtcct	ctcanttnca	caogtgtacg	tttcagttgg	gaagtgcctg	ccattactcc	240
naagcctaga	accttcacgt	cctgaagggt	ctggaagggt	tttcagattg	cttaaganac	300
gcngcccttc	catattcntc	tccactaccc	nggggaacgg	aacaaatgga	gctgcgacng	360
ggaagcgctc	cttcccntcc	gaacgccttc	tttcaaacct	gcctgccttc	cnggcgaatg	420
gaccggaagg	tttncctngc	tcctttcanc	ccnaattact	tcctgngttg	aaaattggcc	480
tgttggtttg	caaatgcngg	aatttggtta	ctttcntcat	gtcctgtgtt	gncnaaccg	540
gctcncctgt	tgccctccctt	tngaaagggt	ttcatcaggg	cccgcctttt	ctcttntaan	600
ngtcctaata	cggncnggac	cactcgggga	aaattttttc	ttttcgaaaa	gccgccccnt	660
cgtccggct						670

<210> 679

<211> 449

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(449)

<223> n = A,T,C or G

<400> 679

actagtccag	tgtggtggaa	ttccattgtg	ttgggagtag	gtctactaca	ncctacttcc	60
cctatcatan	aaganccttan	caacnttcat	gatccccccc	tctannccct	tttcctcanc	120
tgctccttag	tcctgtttgt	cctnttccta	acantcntaa	ganagatnac	taatnctact	180
atctctnacc	tccggaanct	acaanacgtc	tggaactatt	cngaccccat	gcancncat	240
ntcccatcgt	cctcccagcc	cctncccttc	ctttacntta	ctnaacgaag	gtcgacgatc	300
cctccentac	ctcccnnc	attgggnccc	aanggnactg	gacctcacga	ntacaccnac	360
tacggggnga	ctaagnctgn	aactccttac	atatntcccc	gttaccctcn	gaacncagcg	420
aacngcnaca	ccttggacnt	caagaanta				449

<210> 680

<211> 670

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(670)

<223> n = A,T,C or G

<400> 680

tttcngtgtg	gtggaattcg	cggccgcgtc	gacgagaaga	nggaggagga	naaggagaag	60
gagaagaagg	agaanaagga	ggagaaggag	aagaaggaga	agaaatcatc	atcatcatca	120
tccactgtct	ngcaactatt	taagtttgc	antcccttga	aaacaggtag	ttttgtttca	180
atgtttggga	ccactnctga	cnaatgannag	aanaccaata	aatgcttgat	naatgaaaaa	240
nccacttttt	acctgttaga	accctgaggg	taagagaant	gatgtgactc	gacttagtta	300
ccacaaacta	tgatcctagc	atnaattggg	gcactcaca	acctcaactc	cctgtgcaag	360

```

aacagatttt caatgtctac tgatgatttt aaatggatta nttcctctct ttacttctta 420
agggcatgaa gntttatgaa acaaaactat ncagttccag acgcttaacc cacatagtgt 480
taatagtcac cttcaacaca cnactaaacc cccaaaaaan gntttttacg gngtttcgac 540
agttttcttt tctttttgac ttgnttaaca cccnngacaa ctttgtnctn ttcccntgaa 600
tcacancctt cnaanancca atggtncggg tttttctctt tcngggccct tcccttnttn 660
aaaaccanac                                     670

```

```

<210> 681
<211> 494
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(494)
<223> n = A,T,C or G

```

```

<400> 681
tcatgggtgtc cacagtctga tgtgagcgca ttaaatttaa ggatctccgc ctttctcctt 60
aaaactcagg acttggcaat gancctagga agcgcccctc ccctcccan ccanatccaa 120
gccccggacc gctgcgctc cagctgcgcc tagtgaaacc gccgaattcg aattcacact 180
cggngggccg gcgaagggtg gcgcgcccgc gggagcgccg gggcnagccc gagggactgc 240
aagccaanaa nggagggcatg ggtggcgggg ggcgcgctct gatccaggaa ggagcggagg 300
cgccgatcac aactcttna gacgccctgc ccgcgcctgg ccagcgcgca gnetgcagga 360
cgcgcgaggc aggaactcgc tggagtttgc caagcccan gnetctggaa agtntgtagc 420
tccctttcgg ancgnctctt ctggcccttt gggacgggtg tgtcattggg cgggggtctg 480
tataaggggg ggac                                     494

```

```

<210> 682
<211> 263
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(263)
<223> n = A,T,C or G

```

```

<400> 682
tgatcattca agcgnatgnc gnataacgat tgctnagccc aacctttcat agggtcgttc 60
ctttgggaat nggatgtcta ttgaatggca gggatagggg cactcggcat tcgcctctgg 120
tacagttttg catatatatc ctcacgcgca gcgagcgtag ggganagcta agtttgggga 180
aatgccnccg catgnccctn ccggagctta aacccccaac aatnccatt ttnaaaaaag 240
ntttnttant taaaaaaaaa aac                                     263

```

```

<210> 683
<211> 255
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(255)
<223> n = A,T,C or G

```

<400> 683
 cttgcccggc atgcacagac ntnttttacgg acacnctact ccaagngagc ctgnanctgt 60
 ctacgggtcaa nctctaaggt tngncantgc cacanatggc atagtcccga gggcggtnan 120
 tctggantgc tctctgcaact tgaacntaaa gcgcntttca aganaggntct aatngcctgc 180
 ctcttgacaa cnaacaancc cacaccnacc tangaccctn tangcaagga ctggattctg 240
 naaatgcaat acaca 255

<210> 684
 <211> 922
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(922)
 <223> n = A,T,C or G

<400> 684
 acccttcatt tcatgtgctt ctattttctt acatctttta catgactaag ggattaatga 60
 aatcacctct tcataatcat gaccataatt tcatccaaca agtactcaag tttgggtgta 120
 gcactttatt aatgcttacg aattctctct ctctccctct ttctcttttc cttagtccct 180
 gcacaataag gattttttgaa tgtataatat catcttaggt aagctttcat atggtttttg 240
 catatgaagc ttatgactgt cataagccat accaagcctg tggagtatgg catgattttc 300
 attacataat ccaatgaaaa tagacttatt ttaaateccct aactttgtag ttttaatttg 360
 tatttcacta tcttgaaatt aacagctagt acttatccat cacagcagtc tctactgac 420
 atgaagcaag ttgttgaaatg cagtaganca tgaatgaaag catttaatgt tanacaaaaa 480
 tgggtgatac ccaagcattc tgaattatit gcatcaagga atgggacatg tacattagtg 540
 gcatcatttc taccaatatg tgacttgaat tgttttttta aaaaaaggan aatgantttc 600
 tcaatttgct ttaaaaaatt ttnaaaaagt tcaatggcat gctgctttgt ctggacttaa 660
 tttattaaca attnttaanc cttccttaag gacanaattt tgggtgttcag gatcncctg 720
 aagggtctta tttttnatan nattccaaac ccaaaagggtg gtttaaaatg ggnggggttc 780
 ccccnnaaaa atttgaccg gcttttttat atttaaaaaa nttncnttt gngtttgaaa 840
 nctnaatacc aattaagggg gaattttacc tnccagtggg aaaaaaaaaac nctngcctt 900
 naaaaaattc ccnggagnca at 922

<210> 685
 <211> 531
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(531)
 <223> n = A,T,C or G

<400> 685
 tgaggctctg taaaactgtt cctctgctag gcatacttca tattctctat attaaactca 60
 tctttaattg gcatggaaga ttcatgttgc caaatctcag atgaagatcc tatattggat 120
 gcaattaagc ctggcagcgc cctcaaaaaga cagtcttgct actgctagcc acagccagga 180
 cacagtaaca gttccttcta gtgaccnag accataanaa atananatct aaagaattct 240
 gactccaaag gcattagccc attcctggta ttgccaatta tgatagaaaa aattgccaag 300
 ctctgggac atggaaatac actcagtaca tttgagaact ggagaactan tttccaaaat 360
 agtatgaaga catganggtg attgtagata tntgagtttg gagaanttga gggaaatcng 420

attacacatg tttactacaa gagatgttna taagtaaaga aggcctgata tacaatctaa 480
cagacnantg agataaatct taantcacia ctgacntccc ttttggggcg g 531

<210> 686

<211> 336

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(336)

<223> n = A,T,C or G

<400> 686

gngncctna tgagcgcgcg taatacgatc atatagggcg aattgggtac cgggcccccc 60
tcaagaacac tacaagctat gtccctcttct canagagccc tgaantttta acatattgaa 120
agctctnadc ttgccaaana actccactta acttcaaaac acaccctcca cacacatcat 180
gatcaactna gatcttactg aaccagaatc ctnaatggca tacttcagga acaggggtcc 240
anagaagcag ttctcaaant gcagctnaaa aagaaactga aaaccaatt catgcaanac 300
ctagggctta tttgagagca ttttccagtg cagatt 336

<210> 687

<211> 271

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(271)

<223> n = A,T,C or G

<400> 687

aatctgcact ggaaaatgct ctaaaaataag ccctaggtct tgcattgaatt gggtttttcag 60
tttctttttta agctgcactt tgagaactgc ttctctggac ccctgttcct gaagtatgcc 120
atthaggtatt ctgggttcagt aagatctcag ttaatcatga tgtgtgtgga ggggtgtgtt 180
tgaagttnag tggagtctt ttgcaagatc agagctttca atatgttnaa acttcagggc 240
tctctgagaa gaggacatag cttgtagtgt t 271

<210> 688

<211> 740

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(740)

<223> n = A,T,C or G

<400> 688

tgatgaagcg cgcgtnttac nactcactat nggggcgaan tatgggtacc gggnccccct 60
cgaagcggcc gccctttttt tntttttttg tgagagttaa aataaaatat ttgagttaa 120
tttaaagtgt gagtttaatt aaaatatatg gcataatcca agttgggctt tgcanaaaga 180
acacttctca ggaactgtta gttggtgtac caggaactca gaagggctct gttattaaat 240
atatttgtaa aatgcatgga ttctctgaan atcncctctgc atgtgagcaa cacttacatc 300

ncaaaccaaa	attggcattg	catacatnaa	ccaatatttc	ccaaacattt	ctggttatgg	360
ccccccccc	ttgtgtanta	cttattgctg	ttttttggaa	ccctggggaa	attacttaaa	420
atattcagct	ggaaattaca	ggcgttactt	ttaaggganc	aagaattaca	gtgactccca	480
aaattgcaag	tgttgattac	tatttaagaa	cccaagaatt	tgaaagaaat	tttgaaaagt	540
gaaaacngga	aatnttaaat	gacttctcaa	atnttgaaaa	ctcnggnaaa	catctccact	600
ttggtnccct	tccttttaaaa	attggctaaa	aattntttnt	tatnccacc	ccattggaan	660
tncccccccc	ctggaacaat	tggattcccc	tatttcctaa	aaaacggccn	ccccccccgg	720
ggngaacncc	nacnttttgn					740

<210> 689

<211> 635

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(635)

<223> n = A,T,C or G

<400> 689

actagtccag	tgtggtggaa	ttccattgtg	ttgggattac	atatactttt	agcaattttt	60
aaagaagtgt	acaaagttag	gatgtttcct	gagctctcat	atatctgana	atgtcatttt	120
acatctccgt	cttcacctct	caaaacttct	ttcaattctt	tggctcttaa	tagtaatcaa	180
cacttgcaat	ctggagtcac	tgtaattctt	gtcctcttac	agctacncc	gttatttcca	240
gctgaatatt	tttagttatt	tcccaggggt	ccaaaaaaca	gcaataagta	ctacacaaag	300
ggggtgggcc	ataaccagaa	atgtttggga	aatactggct	catgtatgca	atgccaaatc	360
tggtttgcn	ttgtantgtt	gtcacatgc	agagtgaatc	ttcaaanaat	ccatgcattt	420
tccaaatata	tttaataaca	gggaaccttc	tganttctct	gntacaccaa	ctaacagttc	480
ctgaaaaatg	ttctttctgc	aaaacccaac	ttggggatat	gccatatatt	ttaattaaac	540
tcaaacttta	aattaaactn	caattatttt	atnttaact	cctcaaaaaa	aaaaaaaaaa	600
agggggggcc	cttccaangg	ggggnccggt	tcccc			635

<210> 690

<211> 3923

<212> DNA

<213> Homo sapien

<400> 690

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gaattacaac	acatatactt	agtgtttcaa	tgaacaccaa	gataaataag	tgaagagcta	180
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tactcagtgc	agcaaagaaa	gactacagac	atctcaatgg	caggggtgag	aaataagaaa	300
ggctgctgac	tttaccatct	gaggccacac	atctgctgaa	atggagataa	ttaacatcac	360
tagaaacagc	aagatgacaa	tataatgtct	aagtagtgac	atgtttttgc	acatttccag	420
cccctttaaa	tatccacaca	cacaggaagc	acaaaaggaa	gcacagagat	ccctgggaga	480
aatgcccggc	cgccatcttg	ggtcatcgat	gagcctcgcc	ctgtgctggg	tcccgtttgt	540
gaggaagga	cattagaaaa	tgaattgatg	tgttccttaa	aggatgggca	ggaaaacaga	600
tcctgtttgt	gatatttatt	tgaacgggat	tacagatttg	aaatgaagtc	acaaagttag	660
cattaccaat	gagaggaaaa	cagacgagaa	aatcttgatg	gcttcacaag	acatgcaaca	720
aacaaaatgg	aatactgtga	tgacatgagg	cagccaagct	ggggaggaga	taaccacggg	780
gcagagggtc	aggattctgg	ccctgctgcc	taaaactgtc	gttcataacc	aaatcatttc	840
atattttctaa	ccctcaaaac	aaagctgttg	taatatctga	tctctacggg	tccttctggg	900
cccaacattc	tccatatatc	cagccacact	catttttaat	atttagttcc	cagatctgta	960

<210>	691
<211>	882
<212>	DNA


```

nttatgtaag aaatgtcata tatcttttat tttcttttaa tcaaaataaa tatgactttg      60
agcatcccat cccatgcccc atcctatcag aatggtagga acatcaacac aaataattag      120
taatgcaccg catctacatt cccatgctct ctttacttct tcagcattgc ctaaaggcat      180

```

```

aatacacctt taattaatta attcagcctc ctaatgcaca ttaacaaagc ccctgctaga      240
ctctgtccat aatggnaaac ctgnatgac cttgatatta acantttaag gaatgctcat      300
ggattggtnn cagacttaaa aaattgaggg ggctgaanaa aatctaangg anaaatcatg      360
gaagcatttg cacatattac ata                                              383

```

```

<210> 694
<211> 204
<212> DNA
<213> Homo sapien

```

```

<400> 694
tctcttggct ggtcagcctg aagggtggta atgactcacc aacgctacta atccttcttc      60
actgtccctt atttttttcc ctcccagggt cataactcga ggttaaactc tcttttatac     120
aagaaccctg tctgatgaag catcatttca gaattttaag tcaacttaca aatgtgggat     180
tattcacatc tgagtacaaa tttta                                              204

```

```

<210> 695
<211> 670
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(670)
<223> n = A,T,C or G

```

```

<400> 695
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gaacgggtgac ctccaaaaga tatgtccacc tggaaacctca gaataagatc ttatttggaa     120
tagtctttgt agatgtcagt aaggtaaaga tttggagatg agaccctcct ggattagggg     180
agggccctagg tccactggca ggtgtgcttc tcaggggtctg aaaggggaag acagggccac     240
ccagaggagg agacggaggc agagacaggg ccacccagag gaggagacgg aggcagagac     300
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ggcagagaca gggccaccca gaggaggaga cggaggcaga gacagggcca cccaaaggag     420
gagacggagg cagaanacag gcccccccaa agaaganacc ggaggcanaa aacagggcca     480
cccanaggag gagacggagg canaaacagg gccaccccaa aggaggagac ggaggcaaaa     540
cagggccacc caaaaggagg aagccggaag gaaaaaacag ggcccccca aaggaggaag     600
ncggagggcn aaaaanaggg ccccccccaa agngagaaaa ccnggnaggc nanaaaaccn     660
ggggcccnnc                                              670

```

```

<210> 696
<211> 317
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(317)
<223> n = A,T,C or G

```

```

<400> 696
tgaccgcgtt tttctgcaaa ggagagtggg gaaggagggn tgggaagaca aaagttacat      60
gtagcagagg aagagaacag aattttatcc acccttatct ctttagtgag tgaacaaaca     120
gccactgtc atcgtggata catttcactt ttttcacatg actaaggagc tctccggagt     180

```

gaagagtgag	taaatatgtt	tattacgcat	tcatttgcta	agaatcatca	agaacccaaa	240
gtagagacg	tttcgtgggt	gaactttctc	cctactgtct	agtagaatta	tatggggatt	300
ctggatctgc	tggtgcc					317

<210> 697
 <211> 246
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(246)
 <223> n = A,T,C or G

<400> 697						
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tttttttct	tnacagagnt	ntttttgtgc	ccttggttct	tatgctcana	ctcngcaaaa	180
aanatcaaaa	gntacnnatg	aaaaacntat	nccatctnca	naaaggaggt	gnagntatta	240
ctttct						246

<210> 698
 <211> 3674
 <212> DNA
 <213> Homo sapien

<400> 698						
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agccagtga	acataattcct	tcttctctcc	atcaggccaa	atcacgggtg	tgaccttggc	180
cacatcaatg	tcttagaact	tcttcacagc	ctgtttgate	tggtgcttgt	tggtcttaac	240
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caacctacaa gctctctaat catgctcacc taaaagattc ccgggatcta ataggctcaa 1680
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aaaaaaaaaa aaaa 3674

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<210> 699

<211> 2051

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(2051)

<223> n = A,T,C or G

<400> 699

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gtgtcaggag ccaggtctc cagctggang gaacgtcaac cctgcagtgg gagcaggggc 360
cctttgcaca tcctaggcac agatggtaat gtagacacca caggtaagct gggcttggtg 420

```

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cctacccctc cccggattca gaaagaaacc aaacaaggag ctttgtgtgg aatgaaacct 480
cctttcctcc cagaagcact gctgactgtt tgggtggtgc catttgtggc agtgagccct 540
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caccctgcag gaatgccagt gaacatattg ctgacatctt ggagctcagt acctcatagt 720
gtaacggcgt cagtagatct gcctgtgctg ggacttcctg tactacccat tcctgagggg 780
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aaaaaaaaa a 2051

```

<210> 700

<211> 2841

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(2841)

<223> n = A,T,C or G

<400> 700

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<210> 701

<211> 3228

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(3228)

<223> n = A,T,C or G

<400> 701

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ccttgtgaga cactttatcc cagcacttta ggaatactga ggtcatacca gccacatctt 360
atatgcaaga ttgccagca gagatcaggt ccgagagttc ccttttttaa aaaaggagac 420
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<212> PRT

<213> Homo sapiens

<400> 706

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Tyr Leu Ala Ser Val Ala Ala Phe Pro Val Ala Ala Gly Ala Thr Cys
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Leu Ser His Ser Val Ala Val Val Thr Ala Ser Ala Ala Leu Thr Gly
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Phe Thr Phe Ser Ala Leu Gln Ile Leu Pro Tyr Thr Leu Ala Ser Leu
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Tyr His Arg Glu Lys Gln Val Leu Ile Gly Gln Trp Val Glu Ser Gly
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Trp Glu Gly Trp Ser Gly Phe Leu Gly Gly Gln Leu Ala Gln Asn Leu
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Val Ser Gly Lys Gln Leu Trp Arg Met Leu Leu
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<210> 707

<211> 150

<212> PRT

<213> Homo sapiens

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<400> 707

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Ala Ala Gly Ile Thr Tyr Val Pro Pro Leu Leu Leu Glu Val Gly Val
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Glu Glu Lys Phe Met Thr Met Val Leu Gly Glu Ser Leu His Pro Pro
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Ser Phe Leu Phe Gln Ile His Ala Thr Trp His Val Gly Gln Glu Tyr
      65                      70                      75                      80

Leu Cys Pro Gly Ser Cys Leu Glu Gly Glu Val Val Cys Trp Glu Gly
      85                      90                      95

Ile Ala Gly Gln Glu Gly Asp Pro Gly Leu Arg Gly His Thr Lys Arg
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Lys Lys Arg Ile Pro Arg Thr Tyr Pro Ser His Leu Trp Ile Pro Gly
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<212> PRT

<213> Homo sapiens

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Ile Gly Pro Val Leu Gly Leu Val Cys Val Pro Leu Leu Gly Ser Ala
      35                      40                      45

Ser Asp His Trp Arg Gly Arg Tyr Gly Arg Arg Arg Pro Phe Ile Trp
      50                      55                      60

Ala Leu Ser Leu Gly Ile Leu Leu Ser Leu Phe Leu Ile Pro Arg Ala
      65                      70                      75                      80

Gly Trp Leu Ala Gly Leu Leu Cys Pro Asp Pro Arg Pro Leu Glu Leu

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<210> 712
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 <211> 172
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(172)
 <223> n=A,T,C or G

<400> 713
 nntgggtcgcc tgnngcgtnta ctctaaagga tntactatnc atatggantc naanacgact 60
 cactacacgg cncctnccg agcnnnggtc agtgcctnct nggagacctt ctctggggca 120
 ggangagcac tnggtatggt cacgtatcnc ttentaaana tacnccctc cg 172

<210> 714
 <211> 112
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(714)
 <223> n=A,T,C or G

<400> 714
 nntgcgtgcc tggacgtnta ctctgcanga tctactactc atnggaattc taantacgga 60
 ctcactatnc ggcanccgag gcgcagcagg gaanggggtca cctcccagtc tc 112

<210> 715
 <211> 326
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(326)
 <223> n=A,T,C or G

<400> 715
 tactctanag gatctnccng tcatntggat tctatntcga ctactctag ggctcnagcn 60
 gtcngccggg caagttattc ggatcgctcg gntccgagct tcgcaattaa ntgtgccatc 120
 gttctncaac gttcctgact nggaancccc ngcngttcng atccnccngt acctagctcc 180

```
<210> 716
<211> 122
<212> DNA
<213> Homo sapiens
```

```
<400> 716
nntgcgtcgc ctgngcgtn t actctagatg atctgantag tcatatggat tctaatacga 60
ctcannatag ggctctagcg nggatncnga ttctctntcc ngattcantg acnccggtan 120
ca                                                    122
```

```
<220>  
<221> misc_feature  
<222> (1)...(203)  
<223> n=A,T,C or G
```

```
<210> 718
<211> 168
<212> DNA
<213> Homo sapiens
```

```
<400> 718
ggcagganga tcncttgagc ccngagggtc gaggctacag tgagccanga gtgcactact 60
gtnnegccct ccgcatncac gngtggtccg atccccgggt accganctng anttcaactgg 120
antttttttt aancgtnttg antggaacna cctcgantc cctggctg 168
```

```
<210> 719
<211> 210
<212> DNA
<213> Homo sapiens
```

<220>
 <221> misc_feature
 <222> (1)...(210)
 <223> n=A,T,C or G

<400> 719
 cancgctcgc ataacacgta ttttntgatn aagattctna ctgacccatn aantctacnt 60
 ctcaagctct tncanngtcc agtnaangga atgtgtatnn gtnggggatnc cacanaaaaa 120
 aganatntcg gncgcttcat tantcactct tcttaccan ntctctngat nncagnttg 180
 ancntgaacg cacactacng gatntctcca 210

<210> 720
 <211> 131
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(131)
 <223> n=A,T,C or G

<400> 720
 tccatcctaa tacgactcac tatagggctg ccaacctgcc atccactact gaggaagacc 60
 cgnanactta ggggctcact gcgagccacc ggccacaggt cgtatagggc aaagcacgng 120
 gaagcacccc t 131

<210> 721
 <211> 121
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(121)
 <223> n=A,T,C or G

<400> 721
 tccatcctaa tacgactcac tatagggccg ntgantnctg gcgaaaggct tacaattaag 60
 naggaaaaan ganccaacaa ctaaaaaaaa nncggncgtg ncagcttnga tgactngtcc 120
 a 121

<210> 722
 <211> 246
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(246)
 <223> n=A,T,C or G

<400> 722
 anctggagtc gcgcgctgca gtcacattgt ggatccanaa aatcggcaca agctctcntg 60

```

gnttcntcga tatgaanaac actaatccca tgtngtntgn gtctccgtga ttcacccctc 120
gcacnggtcc cnttcnaac cnttgcatag gtgttatgtt gtantctccc cagtgcacaa 180
agattnacac tctctcantg tctganatat gcacgagttc attgtcctgt cnccgtnaac 240
atcaag                                           246

```

```

<210> 723
<211> 160
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(160)
<223> n=A,T,C or G

```

```

<400> 723
cctccggaat atccaantag agtaantncn ctctaatecg gggnaattgg nggggttnnat 60
acgtcctcct cccccagnt aggattnana aaaggntccc cagancaaaa nctccaaagt 120
gnatcnanta gccgtncctg ananccaacg cccctacgtc 160

```

```

<210> 724
<211> 156
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(156)
<223> n=A,T,C or G

```

```

<400> 724
tnanccnata tacaccaaatt tctgattcta aantcccacc caagggaaaa aagttgagaa 60
gagcctttcc acttttctac taataaaaaa atgcaccagg ccctaccann agtgnggaaa 120
acctccttag gcccttgnnt ggaacaancg aaaatc 156

```

```

<210> 725
<211> 347
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(347)
<223> n=A,T,C or G

```

```

<400> 725
aganggttnt atncatgctg tactcgcgcg cctgcagtcg acactagtgg atccaaagaa 60
ttcggcacga gagacggtgc gcgatggacc gagggcccca gccgnggagg cgccgcccgc 120
gagcccgcgg ncagacgccc catcagtagc gtccgcaccg ggnagccgcg gntctcgccc 180
gagccgtggg cgcgcccagag gggcgggctc gcctcccgcc gtccctcgca gctctgcggg 240
gcccgagccc gcgcgctgc cgcgcgcgnc ttgccgctcg gnccgcgagg nccggnaaac 300
gcggtcgagg tctggatgng gcanngcccg cncctntcgc tgagcct 347

```

```

<210> 726

```

<211> 162
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(162)
 <223> n=A,T,C or G

<400> 726
 ttgggtgggt tgggtggggg naaatttncc catttggtg ggtttggggg ggnaaatact 60
 tccgccttt tngtnccca aaganacnaa gggggagtcc cttnatagag gnagnlcat 120
 ncntcncaac nacntngact ttgnccatgg ggagnaaggt gg 162

<210> 727
 <211> 120
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(120)
 <223> n=A,T,C or G

<400> 727
 gtgtgggtgg ggaattccat tgtggttggg ggnaaatctc cgcttggtcca aagnacaggg 60
 ggggtcnctt anagnnagg gggttcctcc ccaccacttg ncttgnccat tngagnaag 120

<210> 728
 <211> 130
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(130)
 <223> n=A,T,C or G

<400> 728
 gaccactgc agcgttnaac ttagcttga ccgagctcgg atccctagtc cgtgtggtgg 60
 aattccatgt gtcgagagag gggcaaatac nctccaanac ancncctca tgctcnacac 120
 atattcgcat 130

<210> 729
 <211> 182
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(182)
 <223> n=A,T,C or G

<400> 729

```

cngactgctn gcgttttaaac ttaagcnagg taccgaacgg ggatnmacga ctantgatcg 60
gctggctgct tccagtcgat tanatttgtg aaaaagctga accncngccn gttaaggggg 120
annatgcaaa anatncatcc nctgccccn taaactgntc tntccnaggg aaaaaangga 180
ag                                                    182

```

```

<210> 730
<211> 678
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(678)
<223> n=A,T,C or G

```

```

<400> 730
cactcncact ccggacctag gcncttcacc actgctctct tctcctcct cctcctctc 60
ctcggggctg ggggaccttc cccagtgaac atctcacttt ggctgaancc cactcggggc 120
agcctgagtt tggggctctt ggcttctca cctcctcgg cccctcctt ggcccgccacc 180
aggccaaacc ggggcagccg taccttgagc ttgtgtccgg cctctccctc cccctctgcc 240
acctggtact cggcatggtt gcccccgga tggcgagagc tccacgtcgg gcagtgagaa 300
gcagaaagta cgctcggccc ctgggggctg ctctcagca cctcgcgcc ccaccctagc 360
tctggcccc agtgtgggca acttcagcct cagcccaacc tcgcctgtgg ccgcctcgcc 420
cgctgtgccc tctcggctta gccccacgtc caactcaagc tggggcactg tcacgggtggg 480
catcttaaag acaccctcac ccaccagcag ctaccacact gcaacctggg ctccaggcaa 540
aaaaagggtc acctggggca nctgaaccct gtacctgctg tgccctctgc tgaanggaat 600
gttatctgaa cctgctgccc tgggggtact gccttcccaa aaccgggtca antccacctg 660
ttggaaggna aatncccc                                                    678

```

```

<210> 731
<211> 135
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(135)
<223> n=A,T,C or G

```

```

<400> 731
gagatccgac gtcaccccc tccggcggcc caagacgctg caactcccga ggcngcccaa 60
atatcttttg aagagcgctc ccagcccaac acaatggaat tccaccacac tggnttagtg 120
gatccgagct aagcc                                                    135

```

```

<210> 732
<211> 660
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(660)
<223> n=A,T,C or G

```

nagtnctatt	tncactaaac	tgngagtgcc	ttaggatggct	ttcaggatgt	cctgaatcct	60
ctataattgt	atacaaaatc	gtgagttttt	aaaaactggg	ttagagctat	tggttctctca	120
gagtctcagg	catcttagac	ccccaaaaag	gttaaggact	actgacttaa	ccaattaggt	180
ttgagtggca	ttggctttga	agaaaagcag	aggaaagata	tattttataa	ttctgggcaa	240


```

caaaaaagtg gatgtgtgcc agcatcttag agtagaatcc tcttaaaagg atagcactgc 300
atatgaacta gtaggtttta accagtgcac atttaggcga agtagctcat ttttctgtta 360
gaattctttt ttatttggga atgggcaagc ttttacagct tttaccttgc caatgaatac 420
ctggaattta aaaaatcttg ttaggcataat tgcccataaa gttttttttc ctagatcata 480
tattcagtaa atatgtttgt agctttatct caatccccc attcattgag gggtgaaaca 540
atgtgaatgg tttgagtgtg gaagctaagt tatttctgtg gaggctaagg gcatttatac 600
caagatatgt tagacttgtg gttcctgtta accattgctg tagacaatag gaattactgt 660
atatccacat ttttaatttt aacatcattc tgctc                                     694

```

<210> 735

<211> 126

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(126)

<223> n=A,T,C or G

<400> 735

```

ncnttgaaac nggttgacca gacttcaggc ctgtgcgctc aatcgtggag aatctcgtgc 60
cgaattcggc acgagtctct ctctctctct ctctctctct ctctctctct ntctctctct 120
ctctctc                                         126

```

<210> 736

<211> 165

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(165)

<223> n=A,T,C or G

<400> 736

```

cagaagcctt taaaccggtt ngaccagact tcaggcctgt gcgctcaatc gtggagaatc 60
tcgtgccgaa ttcggcacga gtctctctct ctctctctct ctctctctct ctctctctct 120
ctctctctct ctctctctct ctctctctct ctctctctct ctctc                                     165

```

<210> 737

<211> 125

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(125)

<223> n=A,T,C or G

<400> 737

```

ggnagcccct ttaaccgttt gtccagactt caggcctgtg cgcctcaatc tggagaatct 60
cgtgccgaat tcggcacgag tctctctctc tctctctctc tctctctctc tctctntctc 120
tctctc                                         125

```

```
<220>
<221> misc_feature
<222> (1)...(739)
<223> n=A,T,C or G
```

<400> 740

```

gntgtcnaaa aagcaggctg gtaccgggtcc ggaattcgcg gccgcgtcga cggcccttgg 60
tgccactagt tctttcattc tccccncca tcaatcagtg aacttttttag cctactcaaa 120
gctttgctcc aatgcatagg atttatgatt gtgggggattt ccagataata taaatattca 180
acatgaatat tttaaattaa ggcattgagac attttttcta actgagcata gccatgaacc 240
tctcacgtct gttcctctgt gncagtttgt agcactgaat acagcagccc tcctaaaagt 300
ccaggcagtg cacagggtctt gacatgatga agtgacgtgt tgctatgggtg attttgcagc 360
tggccaaata gtactgggtt gatttttaccc agcaggagat ttttgcaaaa atttcctggg 420
tgagagtga atcaaaactcc tattttgttt ctctctgca agctgnagtt aanatggatt 480
aatgagtact tttagattaa ttaactctga agagaaaatg ggagaaaagn gaggaagggtt 540
gttggcagaa gtcattgctg gaatccttct gaagggagta ctgacttcac ttgcaaagac 600
aagagactan aagacaatga agttaaactt ggctgtctn tcatatgata gatgcttgag 660
agtacaggnt cagggaaatt ttaattctgn catacgcata ttggattatg tgggtcatgg 720
ctttgtttgg cncctaacc

```

<210> 741

<211> 1171

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(1171)

<223> n=A,T,C or G

<400> 741

```

gccttgnggt gacactatag aacatgtttg tacaaaaaag caggctggta ccgggtccgga 60
attcgcggcc gcgtcgacgg cccttnntgc cactagttct ttcattcttc cccccatca 120
atcagtgaac tttttagcct actcaaagct ttgctccaat gcataggatt tatgattgtg 180
gggatttcca gataatataa atattcaaca tgaatathtt aaattaaggc atgagacatt 240
tttctaact gagcatagcc atgaacctct cacgtctgtt cctctgtgtc agtttgtagc 300
actgaataca gcagccctcc taaaagtcca ggcagtgcac aggtcttgac atgatgaagt 360
gacgtgttgc tatggtgatt ttgcagctgg ccaaatagtc actggttgat tttaccagc 420
aggagatttt tgcaaaaatt tcctgggtga gagtgaatc aaactcctat tttgtttctc 480
ctctgcaagc tgtagttaag aagggattaa tggagtactt tttagaatt aaattaacct 540
cttgaaagaa gaaaaaatgg gggaagaaaa aaagtggag ggaaaagggn ttgggttttg 600
gccnaaaaaa aagttccaan tttnngcntt ggggaaaaat tccccntttt ccttggnaaa 660
aggggggnaa ggttaancct tgggaacctt tttccnncct tttnggccca aaaggggaac 720
ccanggggaa agaaccttta ggnaaaggaa acccattttg gaanggggtt naaaacctnt 780
ngggcccccg ggccctcttc caanaaggga aaaaaaagg cctggaaaan gtaccagggt 840
ttcangggna aaanttaaaa ttcttgacca atancnccat aattgggaat tatggggggg 900
ccatgggctt ttggtttggg cncctaacc cgcnttttaa attcaaanna aaaaaaagn 960
gtttggaaaa nnaaanaaaa aaaattnaan ggnccnnaa aaaaacctg gaaaacctt 1020
ggaaaaaaat tngnnggggg gcnttttgg ttgggggggt tnaaaaaacc ccctnggggg 1080
ttttttaagc ccaaaagggg gggaggggna aaangtnc cttntttttt ttttnngccc 1140
cccttgggga atggnntant tcanggggac c

```

<210> 742

<211> 739

<212> DNA

<213> Homo sapiens

005230"9625950

<220>
 <221> misc_feature
 <222> (1)...(739)
 <223> n=A,T,C or G

<400> 742
 gntgtcnaaa aagcaggctg gtaccgggtcc ggaattcgcg gccgcgtcga cggcccttgg 60
 tgccactagt tctttcattc ttccccncca tcaatcagtg aacttttttag cctactcaaa 120
 gctttgctcc aatgcatagg atttatgatt gtgggggattt ccagataata taaatattca 180
 acatgaatat tttaaattaa ggcatgagac atttttccta actgagcata gccatgaacc 240
 tctcacgtct gttcctctgt gncagtttgt agcactgaat acagcagccc tcctaaaagt 300
 ccaggcagtg cacaggctct gacatgatga agtgacgtgt tgctatggtg attttgcagc 360
 tggccaaaata gtcactgggt gatttttacct agcaggagat ttttgcaaaa atttcctggg 420
 tgagagtga atcaaaactcc tattttgttt ctctctgca agctgnagtt aanatggatt 480
 aatgagtact tttagattaa ttaactctga agagaaaatg ggagaaaagn gaggaagggt 540
 gttggcagaa gtcattgctg gaatccttct gaaggagta ctgacttcac ttgcaaagac 600
 aagagactan aagacaatga agttaaactt ggctgtctn tcatatgata gatgcttgag 660
 agtacaggnt cagggaaatt ttaattctgn catacgcata ttggattatg tgggtcatgg 720
 ctttgtttgg cncctaacc 739

<210> 743
 <211> 610
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(610)
 <223> n=A,T,C or G

<400> 743
 ctgtccttat ttcttttagca aaaatttccc aagagaagaa ttgctgggat aatgcacatt 60
 taaatTTTTG atagacattc ccaaataatta tacctgtttt tgagaccttt aattcctgtt 120
 gtcaaattgc cctatatatg gagtaataaa cacgatttaa agaaatgagg actaaaaaaaa 180
 gattatatat aacccaacat aaaggcaacc tcttaggcgt tgacagaaac tgacaacttt 240
 ttatctgtgg gtgcgatcca ttataagtaa cctgagcacc ttattttttc tttttaaact 300
 ctaggtagga tacccgaggt ccacaaattt ttcataagaa atattttttc tctgccctat 360
 gagattttta aaaatattat actgcttcaa ttgcatcaaa agaaatggac cctaatatct 420
 atgatgaagg atttggagtt agaagacctg agtttcaatt ttggcatggc tgtttgtcta 480
 gctctngat cttggacagg tcaattgact tggcttaatc ttctcatcca tttagnngag 540
 acagcaccac tattcacagg actattgnen gaattaccag acaatagcat aggnngaaaat 600
 ataangcctt 610

<210> 744
 <211> 127
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(127)
 <223> n=A,T,C or G

<400> 744

```

ttnacctccc tggaccgggc ccccttccc cgggcggnct ccccgggctg caggaattct 60
gcacgagggg gagagagttn gagagagaga gagagagaga gagagagaga gagananaga 120
gagagagag                                     127

```

```

<210> 745
<211> 458
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(458)
<223> n=A,T,C or G

```

```

<400> 745
gatatcccg gattcgcggc cgcgtcgacg tggcctctag tttgtcctgg tccaaagcag 60
ggaagctggg ctacgtcctg cccaggtcag ccttaggtta agggctgcct gggggagggg 120
acttctggg ccttcgggtc tctgtgcact ggggtggctc ctgtggccca gaatgccctg 180
gagaagggtc ctactggaag cgaaggtgca gggcagcagg gcctgaggcg caggagctgg 240
tggaggctcc cagcacaggt cgccgcccc gtcacatcac tgctgatggg ggggggactt 300
ggggagtttc ccccgagaat gggaggtctc acagtcccc tgctgcaatg ctgtcggtgc 360
actgngncng caatgtgctc atggncaact gctttttctc tgtggccccg gccgatttat 420
ccagcanngc acccctcttc tncctctcgg anaaagcc                                     458

```

```

<210> 746
<211> 893
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(893)
<223> n=A,T,C or G

```

```

<400> 746
aagcaggctg gtaccgggtc ggaattcgcg gccgcgtcga cgtgggggagt tagctctctg 60
gaccccgctc tagagtaagt catcgataga gcatttgctt gatggggact tccagaaggc 120
cannгааagt cctgccgact tcctggggaa gcccatccgc acgtgggggtg aggggtcccca 180
natggaagca gctgtgtatg cagggagggg gcagaggctg ctgccaatgg gcatgtccct 240
tacctgaaag ggccacctct ccaggtgaca tgtcctgggg gagccggggc cgtctgctcc 300
ggccagaggc gctcagctca ggccacacca ggcaggggcac ctcccaacct ggacagggtg 360
ggaccaaggt ggccttggtc aaaactctct gtgtttgcc aagcaccat cggacacaga 420
gagtcaacca caccacagtc acatggtgtc cacacngcag ggggtcaagg gggccggccc 480
ctccccctca gacgtccctg ggctctggg agtcagcaag gacgaggacg gcattgcctt 540
tcgagacagg aaggagtgta cctcctccc gcggcatcca ggctcngctt ctccggagag 600
gagagggggc tacttgctgg ataaancggc cggggccaca gagaaaaagc aagggtgacca 660
tgagcacctt gcaaacacag tgcaccacc agcatttnag caccngggac tgtgaagacc 720
tcccatttct tcggggggaa acncgcccc ngttcccccc acctcacta gtgnattgtg 780
acctgggggn cgggccgacc cctgtngctt ggggnagccc tccnccagg tttctnnggc 840
ngcccnttaa nggnccctng nttggccctt tggccncctt tncgcttttc cca                                     893

```

```

<210> 747
<211> 738
<212> DNA

```

$\langle 220 \rangle$ $\langle 222 \rangle \quad (1) \dots (738)$

<223> n=A, T, C or G

<400> 747

gatatcccg	gaattcgcg	cgcgctcnac	gaagcacaga	cctgngccct	gctctcatgg	60
ggcagactgc	catttgtcat	tnattactga	aggaaaggga	tcctcagttt	gcttgtggac	120
atttcaaatt	tgaggtgaga	gttggaataag	taagaataaaa	gctgctcttc	aaagagatga	180
atatagaaaa	agaaacaaga	tacagncttg	gcagtaaggc	tgggaggaag	gggaaaagggt	240
aataaagaat	gaaagagtga	gaaatgtgag	caggagctga	acacagaaaa	gttcagnnac	300
agaagcanaa	ggaggggaaga	agggaggagg	gtccctttca	cagaggctca	cgaggatgct	360
ttatgngtgc	catgcagtc	atgttcagga	tgtctgcttc	ttanctctct	acttttctaa	420
tanaaaatttg	gatacttact	gacctaact	atgtaacagg	gagagaagggt	gaatttcaaa	480
gcantaaatt	gaaaaattgt	tcacaatttc	attttttaa	aaaaggaggc	taacagaaga	540
agaggttaat	gtggaatta	tattgatgnt	cttgcgacac	atgaatgnat	ctggatcatc	600
ctgagtggga	ggggagctgt	cttctgacc	caaaaggatc	ctttcggttan	ccngnactta	660
ngtcccaaaa	cctcaccacc	ttggagaaat	natttctctt	tgggggtntc	attaaanct	720
tttggncccc	gcaaaagc					738

<210> 748

<211> 647

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

 $\langle 222 \rangle \quad (1) \dots (647)$

<223> n=A,T,C or G

<400> 748

ctntgtggcg	gtggctgtct	catttgggtg	gacttttttg	gtcgtaggaa	cctggtatng	60
aggtcgagag	taagacgggc	tattagtagt	cgcacgag	ttatttgtga	aaacctggtt	120
agggcctctg	tctccgctgc	gctcgcctaa	attggtatgg	ctcgacttgg	aaacacggtt	180
ctaacacgcg	ttgttagcgc	ccttgctagc	atgtgaagga	cactggccct	accaagaaag	240
attcgagtcg	ctccttcgg	tatcgttcac	ggaggcgata	ttactcttc	ttactacggt	300
tacttcgaga	ttgtctgtga	agtttaagac	tactaaaaag	agtattaagc	ctatcgggaa	360
ttagctagat	cgacacgcta	aaaccaaggg	caatcggcgg	aaatatagag	gcaccaataa	420
tagggcctac	agaaggcccg	aggggttagac	tcacgtttaa	taccggccac	ggggaataa	480
aaaagataaa	gtatcacatcg	tttagcggtc	ctcgaagcc	ttcggtctta	atgcgaagga	540
gtcggaaagca	tcgtcggcga	gtaataaaact	ccatcgcgcc	gagactatct	acgacgccct	600
ccttaanatc	cgtaaattac	tcccggaag	agtatttagg	cggtct		647

<210> 749

$\langle 211 \rangle$ 642

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

 $\langle 222 \rangle \quad (1) \dots (642)$

<223> n=A, T, C or G

ctntgtgtg	gtgngtgtct	catttgggtg	gacttttttg	gtcgtaggaa	cctggatatgc	60
aggtcgcgcg	agcgtgggct	ctcgtcgtgg	atgttggggg	ttggtgtggt	gccggttggt	120
tttggttctg	ttgagcgtag	tgtgtttgaa	ggtagcgtt	cgtgtcttgc	tttgtggttg	180
gtgtttagg	cgggtgggga	ggttgtttgt	tagctgttgt	atgtcatatt	gttgggtgtt	240
ctgcctctgt	ctgtttgtcc	ttggttattg	tggttgttac	ccgcctgtg	tggaaagtgt	300
gtggcagggc	gggaatttaa	gtgggagagt	tgtgggacct	gtggttggtg	ttacgttgct	360
gcttttgtcg	tgggcggtgg	cggcgcgctt	gataattaga	attggatacg	gagtgtataa	420
tacttctagt	aaatggggac	ctagtgtctt	acttcccgga	atagggatct	atgcgaagtc	480
cttaggatag	tcttttgataa	gtttaacgcc	cacgacctta	aaattataca	cgattagacg	540
cataacgact	cctccaggaa	agataaagaa	tctcacatat	agaacgggac	cccatatacg	600
tcggtatagg	aacaagagaa	ctaattttng	ttaaaaagac	tt		642

<213> Homo sapiens

<223> n=A, T, C or G

tttgtggcgg	tgggtgtctca	tttgggtgga	tttttgggtc	gtaggtaacc	tggtatngag	60
gtatagatgc	cgattggtcc	cgacgagcgt	cacgataaat	tcggtagttt	cgcctttttt	120
agaaggcgct	agtactcgga	acttcacttc	atctcggtag	tttacttttg	cgtatatagc	180
cttctccctc	gaagactagc	cgtcacattc	gttccctag	aatcgtttct	gcccctaaga	240
atccgagagc	gagatcccg	aactagagga	accttagaag	agtcgtattt	ccacaaggac	300
cccacagtca	ttccgggaaa	atccctagga	ccatacggtt	aggattcccc	cggaaaccgg	360
agcaaagctc	atgatttccc	acaccgcgag	agcgcctata	accctatccc	atttcttcgg	420
gttatcgagg	atattacgat	caagccgaga	gaaccgctag	aaccgctttc	ttcgctttct	480
cacggaacct	ataagtagaa	agagaaactc	aggtcttaag	ggggcgcttc	ggctaacgaa	540
acttctaact	acgaagagag	tatctagaca	tttaagtcata	aaaatccact	acgcacctcg	600
tgtacgatat	catcgggaqc	qgttcataga	cgggtgtccg			639

<213> Homo sapiens

<223> n=A,T,C or G

cttttgtggc	ggngtgtct	catttgggtg	gatttttggg	tcgtaggnaa	cctggtatng	60
aggcagctct	gagccccc	ccccccccc	ccccccccc	cccccccta	ggnggttggg	120
aanacggtgg	atacctaaat	cgagtngt	cattaaaagt	agttgattac	nccctaaaat	180
aanaanaggg	cttcgtcggg	anaaatcgg	aagganaagt	ctttntggca	tcataanaat	240
actggctcgg	gtcctaana	ntttaaggng	gtnccgagg	gtnttcatac	cgataaaaa	300
cqttttccta	tcggcaacgg	gcttacctga	ggnggactt	ctncggngc	ggngattnan	360

<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(721)
<223> n=A,T,C or G

<400> 754
accggattng tttnctgagcg cgtgactgct aataaaaaag atggantgcc atctttttttt 60
ttnccttgct ttatatatcc agcagcaaaa caaaattggt ctgcngggct ataaaatttg 120
gcttgtagt cntgtacaca actcaggagt gtgacacagc taccagcttt cctcctaact 180
ctcaaggga gaaaattcaa gttctgtcta ggctcactct gtaaagtggg aaacttgctg 240
gttttgtagg ctttttttcc cttcttttcc ctctctcage ttctccctgc ttctcagaan 300
atggagtgt gatgcctgca acttaccaaa tttatctatg aatcagattc cagtgggaga 360
cccctaaagc agaggagaa taaggagtto tccccatgat ggaaaatata caaagacaag 420
gtttcatgga gcaaagaatt ctggctagat ttggtttgta agtggatccc tccccactgc 480
gtgtacactt tatctgtctc tttgcttctt cccacacctc tttcccagct ctctctctgt 540
ctctctcttg ntcccctgac ctttttttct tcccantgca tacttttttn tttccctttt 600
ttaatcttct atantcttaa ncctaccaan gggccctcnt gannaatttn tcaccctga 660
ataggggatt ctntangccc tgagaatttc nttatcanaa aaatattttt ttaaagcatt 720
a 721

<210> 755
<211> 721
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(721)
<223> n=A,T,C or G

<400> 755
accggattng tttnctgagcg cgtgactgct aataaaaaag atggantgcc atctttttttt 60
ttnccttgct ttatatatcc agcagcaaaa caaaattggt ctgcngggct ataaaatttg 120
gcttgtagt cntgtacaca actcaggagt gtgacacagc taccagcttt cctcctaact 180
ctcaaggga gaaaattcaa gttctgtcta ggctcactct gtaaagtggg aaacttgctg 240
gttttgtagg ctttttttcc cttcttttcc ctctctcage ttctccctgc ttctcagaan 300
atggagtgt gatgcctgca acttaccaaa tttatctatg aatcagattc cagtgggaga 360
cccctaaagc agaggagaa taaggagtto tccccatgat ggaaaatata caaagacaag 420
gtttcatgga gcaaagaatt ctggctagat ttggtttgta agtggatccc tccccactgc 480
gtgtacactt tatctgtctc tttgcttctt cccacacctc tttcccagct ctctctctgt 540
ctctctcttg ntcccctgac ctttttttct tcccantgca tacttttttn tttccctttt 600
ttaatcttct atantcttaa ncctaccaan gggccctcnt gannaatttn tcaccctga 660
ataggggatt ctntangccc tgagaatttc nttatcanaa aaatattttt ttaaagcatt 720
a 721

<210> 756
<211> 873
<212> DNA
<213> Homo sapiens

<220>

<400> 756

<210> 757

<211> 782

<212> DNA

<213> Homo sapiens

 $\langle 220 \rangle$

```
<221> misc_feature
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 $\langle 222 \rangle \quad (1) \dots (782)$

<223> n=A,T,C or G

<400> 757

<210> 758

<211> 647

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<223> n=A, T, C or G

ntttgtggcg	gtggtgtctc	atttgggtgg	actttttggg	tctgtagaac	ctggtatnga	60
gggaagagcg	ccgtcgggtc	gagtacagta	tggagtagta	tagtcttcgc	gccttctcgg	120
gcggcggggc	tattctctcc	aaaggcagag	gtccctagtc	gacctcgctc	ccctagggtta	180
ggaacagccg	togaatattt	taggttcgtc	gaggctttct	tccgagctct	acgcctaagt	240
agctccgcga	gcaaagtatc	ggtcattttc	ccctatccat	cactccccta	agtacgcctc	300
attattccgg	aaggcaagag	gccagcattc	ctccttagag	tagagggtag	gtacctccgt	360
cgcgtgccgc	gaaagggcag	agcttcgtgt	cttccctccg	cagcagctta	acggtctacg	420
taggcgtttc	cgatcttttc	acgggaatcg	gggtccggga	gggcggcgga	aaacgtcgac	480
gtctcggtca	ccgtcaccgc	cccgaacaac	tagcggcttt	ccgctttcaa	ctgaggaacc	540
ccgcaccctc	cattagcgct	tacgaatatc	gggngtgat	tgcgcccaatt	cgttagcctt	600
cgataattat	tctctattag	caggtcctatc	tccgcctttc	gatttat		647

<211> 657

<213> Homo sapiens

<221> misc feature

<223> n=A,T,C or G

ctttgtggcg	gtggtgtctc	atttgggttg	actttttggg	tcgtaggaac	ctggtatnga	60
gggctctata	gaaagcctct	tgtctttaga	tacgggcttt	ctggtccttc	gttctggaag	120
tgtagtagta	ggtactgcgg	gaaggcgaag	agtcctttca	aggacgattt	acttaagttg	180
gcttattcta	tagttccttc	gggacataag	gtcggtagca	tctatactgc	gtgggaagct	240
gataggttgg	gacttaaggc	gaataagaag	gaggcggcgg	aggtcgcgat	taccgcagag	300
atattattta	cggcgggccg	gggtaccgcg	ggtcatgcgg	aaattttctg	aggttcttgg	360
attcctaaga	tcgtctccgt	cgagtatact	agcgacgaac	gtaagagtgc	cctcacaaga	420
accggtacaa	actcaagaag	aagttcccat	taagcatcgt	aagaaacggt	aggcagagga	480
cggtaagaag	taatcggaga	aaggtacctc	gtngttacga	agaagcatcg	tnnagctact	540
ttgcgcatacc	gtttatatatt	agacgtgttc	cgtccttctc	cgtgtttana	aaaaggttt	600
attccgacgg	gagacttagg	cgaatggagg	gttcgcgcgt	tganaatcgg	ancgggg	657

<211> 644

<213> Homo sapiens

<221> misc feature

<223> n=A,T,C or G

ctttgtggcg	gtggtgtctc	atttgggtgg	actttttggg	tcgtaggaac	ctggtatgna	60
ggaaaagaag	taagcctcga	agcctatctc	cgaccgtatt	tatttcgcag	aagacggaac	120
tacggacgtc	gttaaccccc	agtagcccc	gtaagaaagg	actaaagcga	atggaaaagt	180
cgggaattcc	ggcggagggg	cggcgattac	tgaaggaggt	aagagtaaga	ctattgcgat	240

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acttgaggcg ttcctcttta aaaggcaccg gaaacactct attaaaaaac acccgaagaa 300
gaacaactca tgcgatcggc cgtgtgcagc cgtcaatagt aaagagagcc atgaaccatg 360
ccatccttag accaattagg atgaagaaga ggaggaagat gaggaccaa ccctaccac 420
tcggaaaacc ccgcacgagc ctccgaacaa aatccgggaa ttaaacggc ggcccacttc 480
cgactctcg tagcgcggac cgaatagaaa accggaaact acagctaaag ggtcctttcc 540
ggcctgttat ctaccacccc gcaatccgat cctccccccc cctcgtccaa aaaccctaac 600
ctctgcggca acattagagc agaaggagag ggcgatccct tgan 644

```

<210> 761

<211> 647

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1) ... (647)

<223> n=A,T,C or G

<400> 761

```

ctttgtggcg gtggtgtctc atttgggtgg actttttggg tcgtaggaac ctggtatnga 60
ggcgggtact ctctgggata atcgggtataa gtgttgtaaa attgggggta agagaaagt 120
tcattataag aagtgggaagc acgagccggg gtgttttagtc gttaatatta agaccggttt 180
ttgttgtagt tataatagctt gcgcgtgggg aggcaataag aaacattgcg ttctgaggcc 240
ggatgcgggg aaccctcttc ggggtctaga gcgcgcgcat tgcaaaataa ggactactga 300
cgccgctcat aacgtactca acaatgagtc ggccctgcatt aagatttcgg cgaagaaccg 360
tactgcgtct actgatagta tattgcattg atagcggcat gagctttatc acgtgtcgtt 420
ttcgggttgt aagaaggag ttaagtogat ctctgaggaa gaagagacc caaataaaaa 480
atgactcaaa aaaacctaga agaaacacga cgaaaggaaa aagaacgtta aaactagtag 540
ctcttcggan gagtagcctt agtagggtaa gtctcctgtg cgtactgtcc taaggtttgg 600
atagcgcggt tgaatagacg gtcacgcgctc agaaggtaaa aanccgg 647

```

<210> 762

<211> 628

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1) ... (628)

<223> n=A,T,C or G

<400> 762

```

cattgtgttg gggtcactga gcccaactttt ttccagattt tttgtaaaat tgtttcgcat 60
tgtgttccct ttattcgctt gtattaatat ttgcgtagtg gattaaacaa atacttggtg 120
ttgactgtca gtcttagagg actgactaga agtagttttc atttggggct caggaaatac 180
ctactttata tttctagcta attaggaaaag tcatttttca gttagggttg tgttttgggt 240
caggcactcg ctagctagat gacctaacat gctacttaat ttctgagtgt ttgtgtccat 300
ccctgtagga ttgttgccgg gttaaatgaa attgtgtata tttgtaaagc atttacctca 360
gtgcccagac tgtgacagag tagattatta ggcttgctct tatttctgtg attaaattta 420
gtgtcagatt agcaacctat agctacttct aaagctgctg ctgctttctt tgtttaggg 480
taggaagaaa catgctggac agtttgccaa atgagagtta catgatgtgg cttgtgggaa 540
cattctaact tggaacttgc ccatttccag gactttgnng ttcanagatt tttggggata 600
gatgtaaggg ttaaaaaaaa cngaaaac 628

```

```
<220>
<221> misc_feature
<222> (1)...(175)
<223> n=A,T,C or G
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<400> 766
cattgtgttg ggcctagtcc gaatactttt agtaacttca gacagatctc ctcattctctt 60
tctggggctt ggntttttctc ctttgtanaa tgatgccttt ctgtgggtttt gtcattttcta 120
acattctgtg ngtgatgagg tgtatatctg anganctcta tcnccanagt actct 175

<210> 767
<211> 602
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(602)
<223> n=A,T,C or G

<400> 767
nnnttttaaaa nctgtntctcc ccgcggtggc ggccgctcta gaactagtgg atccttttcca 60
cctgggtttgt tttcagtgtt taatcctatt agtatcagca ggatataggt caggatatca 120
gggtgcagaac ctgtggaatc agccaatttg gcttgctcat ttactttaat aagggtcccat 180
aatgagttag agtacaaagt tcaagccctg ttgaggggtc gcattaaact ctcagaagta 240
tttagagtgt gccaggagcc gcgaagggtc gggttogggtg gtggcgggaa ctgtattaga 300
gtgctaggca cggcgcgaca aagtctgtcc aacccaaaac ggtgctgagg cgttgggtgt 360
gagctccagt actcagaaaa gcattctcagc aggtactcaa cagatcctca ggggcttggg 420
ggcccagcac tggcagttag ggcatgaaag acataaaaagg gcactacctg tgggtatttt 480
ctgttctcca aggaggaagt agcaaaaatt aggacgctgg aatatcctat gttgtagcaa 540
tcccagaaca actgatgctc aacaaatacc acacaaaaca aattttttta aatttaattct 600
ta 602

<210> 768
<211> 671
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(671)
<223> n=A,T,C or G

<400> 768
tccaccgcgg tggcgggccgc tctagactag tggatccact agtccagtgt ggggtgggaat 60
tcgcggnccg cgtcgacaaa aatactgcta aagtaatat tttatagatg actatttgcc 120
ttggggccag gaaaagcagc tggagttatt cacttagtac cattttttaca tactaacttt 180
gccttttcca tgcttgcttg atgcgggcttg cagcactgaa gaacagtttc aattgctagc 240
caaccagaga gcatgatcaa accaaacaag ttccctgttt caggaaaaac aggttttagg 300
taactgaagg gttaccagtt actgattcca caatcttctc tgtaaaanat ttctgcctat 360
tatgcagact gggcggtttt aaanntggta aaactatnaa ataccatac aatattttta 420
ngggggcccn ttatnaagct tttcaggcct tcccttttcc atagcattgg tgggatacaa 480
gaaaccttta aacagcaacn agctatcnag gcccaaaaagg aaagtaattn tgatttttta 540
nagattccgn aacgaaaaaa tggctgggtt caaatacnac cttcttttta aaatggnttc 600
cttattaaac nttttttttt ttttaatttta ccccatggtc ntgatnttng ngcttccgcc 660
canaaaatng n 671

<210> 769

<211> 877
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(877)
 <223> n=A,T,C or G

<400> 769
 aaagctggag ctccccgcgg tggcggcgcg tctagaacta gtggatccac tagtccanng 60
 ngggggaatt cgcggccgcg tcgacctcta tacctttgnt catgcagctt cctctgactg 120
 ggtttgttct tcaacttggct aacccctctt ttacttaagc acaccttgaa cattccctcc 180
 ttccccattt ccccgccagng cccctaattg acatacttct gaataacaca ggtgggtattc 240
 cttccttgtt ggaacctcct ggaggaagag acagatgatt aacaaatcct tccatcaacc 300
 cctttgacca tgacatcaac agtgctccaa attatggggt accgtattag cctatgtcta 360
 tcttgatcag aatccttacc tcggtgtatt gaaattatct atttcgtgcc tgcctcttta 420
 aagtcagggt ttgccttata tattgtctaa caccatgcag taggtaacat gcagtaggaa 480
 acatggcatt aaattatttg ggttcaaata ccagttatgg tgtgtaaatg cctaccaggc 540
 cgtgaggcac ctgctaagca ggttgccacg atcatttgaa ttcacaccac ctttttgcaa 600
 tagaacagat aggcaacaga ggctcatttg ggctaaagga tttgatggag gggaagtgcc 660
 aggattccca ccaaggcctc anggccagg tccanggacc atgtctgttg tgacaactgg 720
 agtgcatttc atatccccctn ctctgngggg naaggtccct cncgnggaga acnnttaaaa 780
 caatcatntc tnggggggntt aatgcttctt nccccagtg ggtncactgc ngccacgagt 840
 cccanccact agtcccangt ctgtcatgaa ccanccc 877

<210> 770
 <211> 874
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(874)
 <223> n=A,T,C or G

<400> 770
 ctggnctccc cgcggtggcg gccgctctag aactagtgga tccactagtc cagtgtgggtg 60
 gaattcgcgg ccgcgtcgac cttttcaaag gttaacttat ttaattatca canngcaac 120
 ccgatgagta ggtaacagta ttttactgat aggtaatcta aagaaggagg cttaaataaat 180
 tgcccaattt cgaacagtga gaggaagaat taggattgaa acacatatag tggcttcaga 240
 atctgtaacc ctcacgatgc cactactact tctttcagaa taccctttgc ctatctattc 300
 tgttcctatg tcatcaaatt ataactactt taaaaagtat ttgtctttat tattttttaa 360
 aaaacacagg gaagtatttc tgatcagggg cagtattgggt tctgaaagac aagccagtgt 420
 ttttgagggt ttctcccttg ccagtttttc tatgctgggt tattcaagtc ctaagaattg 480
 tgtagctatt acagaaccgc ttttagcaaa gtgttcocatt aatcaagggtg atttataaca 540
 aaatttcac ccaagtttga gtgctctgaa aacatagcca aaatgttcgc agggctctacc 600
 cctctcgtgt gtcccttttt ttttagctatt tcagaagcac actggtgcaa tatttttacga 660
 aatgagtttc ttccccttac ctctgcatcc tctaagaaaa aatcattgnt gttttatgaa 720
 natgaanatc ctgctatttc atatcttgat tggagctgct taattaaatg accatttttna 780
 aatttgtttt gattccnngc aaaaaaagtt tnttnttgga tgtagggggc tcnaaaagnc 840
 caaaaccccc caaaattttt nnttggggaac ccna 874

<210> 771

<211> 156
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(156)
 <223> n=A,T,C or G

<400> 771
 ttaaaaaanct ggnctccccg cgggtggcggc cgctctagaa ctagtggatc cactagtcca 60
 gtgtggtgga attcgcggcc gcgtcgaccg cgagcggtcg cccttttttt ttttttttn 120
 ngtttttttg aanaattcat tgggtattta ttatc 156

<210> 772
 <211> 586
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(586)
 <223> n=A,T,C or G

<400> 772
 ncaanctggn ctccaccgcg gtggcggcgg ctctagacta gtggatccac tagtccagtg 60
 tgggtggaatt cgcggccgcg tcgatcaca agtgctcaca agtcnngnat ttattttatc 120
 tccagatatg aaacttaccc ccagctatgg tcttctatct gttatttaatt ttctaggcca 180
 attttttcca cttgaatgtc agtattttta ttcaaagtca ccttggtccaa ataccaagtc 240
 atcaacttac cctcaaatta tatcctcatt cagaaaaatc acatctatta atggtagcta 300
 ttttatccct gccccctgct ttttcttttt atattttaatt aatttgntca tccagcaaat 360
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<212> PRT
<213> Homo sapiens
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Cys	Leu 690	Phe	Ile	Ile	Pro	Leu 695	Val	Gly	Cys	Gly	Phe 700	Val	Ser	Phe	Arg
Lys 705	Lys	Pro	Val	Asp	Lys 710	His	Lys	Lys	Leu	Leu 715	Trp	Tyr	Tyr	Val	Ala 720
Phe	Phe	Thr	Ser	Pro 725	Phe	Val	Val	Phe	Ser 730	Trp	Asn	Val	Val	Phe 735	Tyr
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<212> DNA

<213> Homo sapiens

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<400> 780

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Gln Ser Gln His Met Glu Gly Thr Gln Ile Asn Gln Ser Glu Lys Trp
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 Lys Ala Ile Asn Thr Ser Ile Lys Asn Lys Ile Pro Cys Val Val Val
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 325 330 335
 Glu Asp Ala Leu Thr Ser Ser Ala Val Lys Glu Lys Leu Val Arg Phe
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 Leu Pro Arg Thr Val Ser Arg Leu Pro Glu Glu Glu Thr Glu Ser Trp
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 Ile Lys Met Glu Glu Ala Gly Asp Glu Ile Val Ser Asn Ala Ile Ser
 385 390 395 400
 Tyr Ala Leu Tyr Lys Ala Phe Ser Thr Ser Glu Gln Asp Lys Asp Asn
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 Ala Asn Asp Glu Ile Phe Thr Asn Asp Arg Arg Trp Glu Ser Ala Asp
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Gln	His	Phe	Ile 660	Ala	Gln	Pro	Gly	Val 665	Gln	Asn	Phe	Leu	Ser	Lys	Gln
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Phe	Phe	Thr	Ser	Pro 725	Phe	Val	Val	Phe	Ser 730	Trp	Asn	Val	Val	Phe	Tyr 735
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Phe 785	Thr	Asp	Leu	Trp	Asn 790	Val	Met	Asp	Thr	Leu 795	Gly	Leu	Phe	Tyr	Phe 800
Ile	Ala	Gly	Ile	Val	Phe	Arg	Leu	His	Ser	Ser	Asn	Lys	Ser	Ser	Leu

805 810 815
 Tyr Ser Gly Arg Val Ile Phe Cys Leu Asp Tyr Ile Ile Phe Thr Leu
 820 825 830
 Arg Leu Ile His Ile Phe Thr Val Ser Arg Asn Leu Gly Pro Lys Ile
 835 840 845
 Ile Met Leu Gln Arg Met Leu Ile Asp Val Phe Phe Phe Leu Phe Leu
 850 855 860
 Phe Ala Xaa Trp Met Val Ala Phe Gly Val Ala Arg Gln Gly Ile Leu
 865 870 875 880
 Arg Gln Asn Glu Gln Arg Trp Arg Trp Ile Phe Arg Ser Val Ile Tyr
 885 890 895
 Glu Pro Tyr Leu Ala Met Phe Gly Gln Val Pro Ser Asp Val Asp Gly
 900 905 910
 Thr Thr Tyr Asp Phe Ala His Cys Thr Phe Thr Gly Asn Glu Ser Lys
 915 920 925
 Pro Leu Cys Val Glu Leu Asp Glu His Asn Leu Pro Arg Phe Pro Glu
 930 935 940
 Trp Ile Thr Ile Pro Leu Val Cys Ile Tyr Met Leu Ser Thr Asn Ile
 945 950 955 960
 Leu Leu Val Asn Leu Leu Val Ala Met Phe Gly Tyr Thr Val Gly Thr
 965 970 975
 Val Gln Glu Asn Asn Asp Gln Val Trp Lys Phe Gln Arg Tyr Phe Leu
 980 985 990
 Val Gln Glu Tyr Cys Ser Arg Leu Asn Ile Pro Phe Pro Phe Ile Val
 995 1000 1005
 Phe Ala Tyr Phe Tyr Met Val Val Lys Lys Cys Phe Lys Cys Cys Cys
 1010 1015 1020
 Lys Glu Lys Asn Met Glu Ser Ser Val Cys Cys Phe Lys Asn Glu Asp
 1025 1030 1035 1040
 Asn Glu Thr Leu Ala Trp Glu Gly Val Met Lys Glu Asn Tyr Leu Val
 1045 1050 1055
 Lys Ile Asn Thr Lys Ala Asn Asp Thr Ser Glu Glu Met Arg His Arg
 1060 1065 1070
 Phe Arg Gln Leu Asp Thr Lys Leu Asn Asp Leu Lys Gly Leu Leu Lys
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006260 "GCTGGG"

1090

1095

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<211> 15

<212> PRT

<213> Homo sapiens

<400> 781

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 5 10 15

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<211> 45

<212> DNA

<213> Homo sapiens

<400> 782

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<210> 784

<211> 45

<212> DNA

<213> Homo sapiens

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<210> 785

<211> 45

<212> DNA

<213> Homo sapiens

<400> 785

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<210> 786

<211> 45

<212> DNA

<213> Homo sapiens

<400> 786

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005230 "3621590

<400> 793

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<210> 795
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<212> DNA
<213> Homo sapiens

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<210> 796
<211> 45
<212> DNA
<213> Homo sapiens

<400> 796
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<210> 797
<211> 45
<212> DNA
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<400> 797
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<210> 798
<211> 45
<212> DNA
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<400> 798
agacccttgc tcgctaacga cctcatgctc atcaagttgg acgaa 45

<210> 799
<211> 15
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<213> Homo sapiens

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5 10 15

<210> 800
<211> 15

<212> PRT

<213> Homo sapiens

<400> 800

Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val Glu Ala Ser Leu
 5 10 15

<210> 801

<211> 15

<212> PRT

<213> Homo sapiens

<400> 801

Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met
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<210> 802

<211> 15

<212> PRT

<213> Homo sapiens

<400> 802

Tyr Thr Ile Gly Leu Gly Leu His Ser Leu Glu Ala Asp Gln Glu
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<210> 803

<211> 14

<212> PRT

<213> Homo sapiens

<400> 803

Phe Gln Asn Ser Tyr Thr Ile Gly Leu Gly Leu His Ser Leu
 5 10

<210> 804

<211> 15

<212> PRT

<213> Homo sapiens

<400> 804

Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu
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<210> 805

<211> 15

<212> PRT

<213> Homo sapiens

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006030 "364360"

His Pro Gln Trp Val Leu Ser Ala Ala His Cys Phe Gln Asn Ser
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 Ser Gly Val Leu Val His Pro Gln Trp Val Leu Ser Ala Ala His
 5 10 15

<210> 807
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 Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln Trp Val
 5 10 15

<210> 808
 <211> 15
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<400> 808
 Ala Leu Val Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val
 5 10 15

<210> 809
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 <212> PRT
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<400> 809
 Ser Gln Pro Trp Gln Ala Ala Leu Val Met Glu Asn Glu Leu Phe Cys
 5 10 15

Ser

<210> 810
 <211> 15
 <212> PRT
 <213> Homo sapiens

<400> 810
 Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly Asn Ser Cys Leu

005230 "3c2f5950"

<210> 816
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 <212> DNA
 <213> Artificial Sequence

<220>
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<400> 816
 ccgctcaggt ccacccaag cttcacagg

29

<210> 817
 <211> 1959
 <212> DNA
 <213> Homo sapiens

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 aagaaacgag aatgtgtctt ctttaccaaa gattccaagg ccacggagaa tgtgtgcaag 180
 tgtggctatg cccagagcca gcacatggaa ggcaccaga tcaaccaaag tgagaaatgg 240
 aactacaaga aacacaccaa ggaatttctt accgacgcct ttggggatat tcagtttgag 300
 acactgggga agaaaaggaa gtatatacgt ctgtcctgag acacggacgc ggaaatcctt 360
 tacgagctgc tgaccacgca ctggcacctg aaaacaccca acctgggtcat ttctgtgacc 420
 gggggcgcca agaacttcgc cctgaagccg cgcagtcgca agatcttcag ccggtcatc 480
 tacatcgccg agtccaaagg tgcttggtt ctacggggag gcacccatta tggcctgatg 540
 aagtacatcg gggaggtggt gagagataac accatcagca ggagttcaga ggagaatatt 600
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 ctgtatatcc tggacaacaa ccacacacat ttgctgctcg tggacaatgg ctgtcatgga 780
 catccactg tccaagcaaa gctccggaat cagctagaga agtatatctc tgagcgcatc 840
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 cagatcgcca agaattccta taatgatgcc ctctcacgt ttgtctggaa actggttgcg 1560
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 gctgctgggg agtccgagga gctggctaag gagtacgaga cccgggctgt tgagctgttc 1860
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<210> 818
 <211> 652

<212> PRT

<213> Homo sapiens

<400> 818

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Met Arg Asn Arg Arg Asn Asp Thr Leu Asp Ser Thr Arg Thr Leu Tyr
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      20                      25                      30

Val Asn Phe Ile Gln Ala Asn Phe Lys Lys Arg Glu Cys Val Phe Phe
      35                      40                      45

Thr Lys Asp Ser Lys Ala Thr Glu Asn Val Cys Lys Cys Gly Tyr Ala
      50                      55                      60

Gln Ser Gln His Met Glu Gly Thr Gln Ile Asn Gln Ser Glu Lys Trp
      65                      70                      75                      80

Asn Tyr Lys Lys His Thr Lys Glu Phe Pro Thr Asp Ala Phe Gly Asp
      85                      90                      95

Ile Gln Phe Glu Thr Leu Gly Lys Lys Gly Lys Tyr Ile Arg Leu Ser
      100                     105                     110

Cys Asp Thr Asp Ala Glu Ile Leu Tyr Glu Leu Leu Thr Gln His Trp
      115                     120                     125

His Leu Lys Thr Pro Asn Leu Val Ile Ser Val Thr Gly Gly Ala Lys
      130                     135                     140

Asn Phe Ala Leu Lys Pro Arg Met Arg Lys Ile Phe Ser Arg Leu Ile
      145                     150                     155                     160

Tyr Ile Ala Gln Ser Lys Gly Ala Trp Ile Leu Thr Gly Gly Thr His
      165                     170                     175

Tyr Gly Leu Met Lys Tyr Ile Gly Glu Val Val Arg Asp Asn Thr Ile
      180                     185                     190

Ser Arg Ser Ser Glu Glu Asn Ile Val Ala Ile Gly Ile Ala Ala Trp
      195                     200                     205

Gly Met Val Ser Asn Arg Asp Thr Leu Ile Arg Asn Cys Asp Ala Glu
      210                     215                     220

Gly Tyr Phe Leu Ala Gln Tyr Leu Met Asp Asp Phe Thr Arg Asp Pro
      225                     230                     235                     240

Leu Tyr Ile Leu Asp Asn Asn His Thr His Leu Leu Leu Val Asp Asn
      245                     250                     255

Gly Cys His Gly His Pro Thr Val Glu Ala Lys Leu Arg Asn Gln Leu
      260                     265                     270

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Glu Lys Tyr Ile Ser Glu Arg Thr Ile Gln Asp Ser Asn Tyr Gly Gly
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 Lys Ile Pro Ile Val Cys Phe Ala Gln Gly Gly Gly Lys Glu Thr Leu
 290 295 300
 Lys Ala Ile Asn Thr Ser Ile Lys Asn Lys Ile Pro Cys Val Val Val
 305 310 315 320
 Glu Gly Ser Gly Gln Ile Ala Asp Val Ile Ala Ser Leu Val Glu Val
 325 330 335
 Glu Asp Ala Leu Thr Ser Ser Ala Val Lys Glu Lys Leu Val Arg Phe
 340 345 350
 Leu Pro Arg Thr Val Ser Arg Leu Pro Glu Glu Glu Thr Glu Ser Trp
 355 360 365
 Ile Lys Trp Leu Lys Glu Ile Leu Glu Cys Ser His Leu Leu Thr Val
 370 375 380
 Ile Lys Met Glu Glu Ala Gly Asp Glu Ile Val Ser Asn Ala Ile Ser
 385 390 395 400
 Tyr Ala Leu Tyr Lys Ala Phe Ser Thr Ser Glu Gln Asp Lys Asp Asn
 405 410 415
 Trp Asn Gly Gln Leu Lys Leu Leu Leu Glu Trp Asn Gln Leu Asp Leu
 420 425 430
 Ala Asn Asp Glu Ile Phe Thr Asn Asp Arg Arg Trp Glu Ser Ala Asp
 435 440 445
 Leu Gln Glu Val Met Phe Thr Ala Leu Ile Lys Asp Arg Pro Lys Phe
 450 455 460
 Val Arg Leu Phe Leu Glu Asn Gly Leu Asn Leu Arg Lys Phe Leu Thr
 465 470 475 480
 His Asp Val Leu Thr Glu Leu Phe Ser Asn His Phe Ser Thr Leu Val
 485 490 495
 Tyr Arg Asn Leu Gln Ile Ala Lys Asn Ser Tyr Asn Asp Ala Leu Leu
 500 505 510
 Thr Phe Val Trp Lys Leu Val Ala Asn Phe Arg Arg Gly Phe Arg Lys
 515 520 525
 Glu Asp Arg Asn Gly Arg Asp Glu Met Asp Ile Glu Leu His Asp Val
 530 535 540
 Ser Pro Ile Thr Arg His Pro Leu Gln Ala Leu Phe Ile Trp Ala Ile
 545 550 555 560

Leu Gln Asn Lys Lys Glu Leu Ser Lys Val Ile Trp Glu Gln Thr Arg
 565 570 575
 Gly Cys Thr Leu Ala Ala Leu Gly Ala Ser Lys Leu Leu Lys Thr Leu
 580 585 590
 Ala Lys Val Lys Asn Asp Ile Asn Ala Ala Gly Glu Ser Glu Glu Leu
 595 600 605
 Ala Asn Glu Tyr Glu Thr Arg Ala Val Glu Leu Phe Thr Glu Cys Tyr
 610 615 620
 Ser Ser Asp Glu Asp Leu Ala Glu Gln Leu Leu Val Tyr Ser Cys Glu
 625 630 635 640
 Ala Trp Gly Gly Leu Glu His His His His His His
 645 650

<210> 819
 <211> 132
 <212> PRT
 <213> Homo sapien

<400> 819
 Thr Ala Ala Ser Asp Asn Phe Gln Leu Ser Gln Gly Gly Gln Gly Phe
 1 5 10 15
 Ala Ile Pro Ile Gly Gln Ala Met Ala Ile Ala Gly Gln Ile Arg Ser
 20 25 30
 Gly Gly Gly Ser Pro Thr Val His Ile Gly Pro Thr Ala Phe Leu Gly
 35 40 45
 Leu Gly Val Val Asp Asn Asn Gly Asn Gly Ala Arg Val Gln Arg Val
 50 55 60
 Val Gly Ser Ala Pro Ala Ala Ser Leu Gly Ile Ser Thr Gly Asp Val
 65 70 75 80
 Ile Thr Ala Val Asp Gly Ala Pro Ile Asn Ser Ala Thr Ala Met Ala
 85 90 95
 Asp Ala Leu Asn Gly His His Pro Gly Asp Val Ile Ser Val Asn Trp
 100 105 110
 Gln Thr Lys Ser Gly Gly Thr Arg Thr Gly Asn Val Thr Leu Ala Glu
 115 120 125
 Gly Pro Pro Ala
 130

<210> 820
 <211> 36
 <212> DNA
 <213> Artificial Sequence

<220>

<223> PCR primer

<400> 820

ggggaattca tgatccggga gaaatttgcc cactgc 36

<210> 821

<211> 33

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer

<400> 821

gggctcgagt caggagtttg agaccagcct ggc 33

<210> 822

<211> 675

<212> DNA

<213> Homo sapiens

<400> 822

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atgcatcacc atcaccatca cacggccgcg tccgataact tccagctgtc ccaggggtggg 60
cagggaattcg ccattccgat cgggcaggcg atggogatcg cgggccagat caagcttccc 120
accgttcata tcgggcctac cgccttctct ggcttgggtg ttgtcgacaa caacggcaac 180
ggcgacgag tccaacgctt ggtcgggagc gctccggcgg caagtctcgg catctccacc 240
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gcgtttaacg ggcatcatcc cgggtgacgtc atctcggtga cctggcaaac caagtcgggc 360
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gagaaatttg cccactgcac cgtgctaacc attgcacaca gattgaacac cattattgac 480
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gccgtgccc tctactgaaac agcaaaacag agatgggggt tcaccatgtt ggccaggctg 660
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<210> 823

<211> 291

<212> DNA

<213> Homo sapiens

<400> 823

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atggggatcc gggagaaatt tgcccactgc accgtgctaa ccattgcaca cagattgaac 60
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gagccgtatg ttttgctgca aaataaagag agcctatttt acaagatggg gcaacaactg 180
ggcaaggcag aagccgctgc cctcactgaa acagcaaaac agagatgggg ttccaccatg 240
ttggccaggc tgggtctcaaa ctccctcgag caccaccacc accaccactg a 291
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<210> 824

<211> 1074

<212> DNA

<213> Homo sapiens

<400> 824

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ttgctacttg atgagatatc acagcgcaac cgtcagctgc cgtcagatgg taaaaagatg 120
gtgcatgtgc aggattttac tgcttttttg gataaggcat cagagacccc aactctacaa 180
ggcctttcct ttactgtcag acctggcgaa ttgttagctg tggtcggccc cgtgggagca 240
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agcgtgcatg gaagaattgc ctatgtgtct cagcagccct ggggtgttctc gggaactctg 360
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gcttggtgctc tgaaaaagga tttacagctg ttggaggatg gtgatctgac tgtgatagga 480
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aaccgttctg aaggaaaagt tggttttcag gcctataaga attacttcag agctgggtgct 1020
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<210> 825

<211> 224

<212> PRT

<213> Homo sapiens

<400> 825

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Met His His His His His Thr Ala Ala Ser Asp Asn Phe Gln Leu
      5              10              15

Ser Gln Gly Gly Gln Gly Phe Ala Ile Pro Ile Gly Gln Ala Met Ala
      20              25              30

Ile Ala Gly Gln Ile Lys Leu Pro Thr Val His Ile Gly Pro Thr Ala
      35              40              45

Phe Leu Gly Leu Gly Val Val Asp Asn Asn Gly Asn Gly Ala Arg Val
      50              55              60

Gln Arg Val Val Gly Ser Ala Pro Ala Ala Ser Leu Gly Ile Ser Thr
      65              70              75              80

Gly Asp Val Ile Thr Ala Val Asp Gly Ala Pro Ile Asn Ser Ala Thr
      85              90              95

Ala Met Ala Asp Ala Leu Asn Gly His His Pro Gly Asp Val Ile Ser
      100             105             110

Val Thr Trp Gln Thr Lys Ser Gly Gly Thr Arg Thr Gly Asn Val Thr
      115             120             125

Leu Ala Glu Gly Pro Pro Ala Glu Phe Met Ile Arg Glu Lys Phe Ala
      130             135             140

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His Cys Thr Val Leu Thr Ile Ala His Arg Leu Asn Thr Ile Ile Asp
 145 150 155 160

Ser Asp Lys Ile Met Val Leu Asp Ser Gly Arg Leu Lys Glu Tyr Asp
 165 170 175

Glu Pro Tyr Val Leu Leu Gln Asn Lys Glu Ser Leu Phe Tyr Lys Met
 180 185 190

Val Gln Gln Leu Gly Lys Ala Glu Ala Ala Ala Leu Thr Glu Thr Ala
 195 200 205

Lys Gln Arg Trp Gly Phe Thr Met Leu Ala Arg Leu Val Ser Asn Ser
 210 215 220

<210> 826

<211> 357

<212> PRT

<213> Homo sapiens

<400> 826

Met Ser Ala Ile Glu Arg Val Ser Glu Ala Ile Val Ser Ile Arg Arg
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 20 25 30

Leu Pro Ser Asp Gly Lys Lys Met Val His Val Gln Asp Phe Thr Ala
 35 40 45

Phe Trp Asp Lys Ala Ser Glu Thr Pro Thr Leu Gln Gly Leu Ser Phe
 50 55 60

Thr Val Arg Pro Gly Glu Leu Leu Ala Val Val Gly Pro Val Gly Ala
 65 70 75 80

Gly Lys Ser Ser Leu Leu Ser Ala Val Leu Gly Glu Leu Ala Pro Ser
 85 90 95

His Gly Leu Val Ser Val His Gly Arg Ile Ala Tyr Val Ser Gln Gln
 100 105 110

Pro Trp Val Phe Ser Gly Thr Leu Arg Ser Asn Ile Leu Phe Gly Lys
 115 120 125

Lys Tyr Glu Lys Glu Arg Tyr Glu Lys Val Ile Lys Ala Cys Ala Leu
 130 135 140

Lys Lys Asp Leu Gln Leu Leu Glu Asp Gly Asp Leu Thr Val Ile Gly

145 150 155 160
 Asp Arg Gly Thr Thr Leu Ser Gly Gly Gln Lys Ala Arg Val Asn Leu
 165 170 175
 Ala Arg Ala Val Tyr Gln Asp Ala Asp Ile Tyr Leu Leu Asp Asp Pro
 180 185 190
 Leu Ser Ala Val Asp Ala Glu Val Ser Arg His Leu Phe Glu Leu Cys
 195 200 205
 Ile Cys Gln Ile Leu His Glu Lys Ile Thr Ile Leu Val Thr His Gln
 210 215 220
 Leu Gln Tyr Leu Lys Ala Ala Ser Gln Ile Leu Ile Leu Lys Asp Gly
 225 230 235 240
 Lys Met Val Gln Lys Gly Thr Tyr Thr Glu Phe Leu Lys Ser Gly Ile
 245 250 255
 Asp Phe Gly Ser Leu Leu Lys Lys Asp Asn Glu Glu Ser Glu Gln Pro
 260 265 270
 Pro Val Pro Gly Thr Pro Thr Leu Arg Asn Arg Thr Phe Ser Glu Ser
 275 280 285
 Ser Val Trp Ser Gln Gln Ser Ser Arg Pro Ser Leu Lys Asp Gly Ala
 290 295 300
 Leu Glu Ser Gln Asp Thr Glu Asn Val Pro Val Thr Leu Ser Glu Glu
 305 310 315 320
 Asn Arg Ser Glu Gly Lys Val Gly Phe Gln Ala Tyr Lys Asn Tyr Phe
 325 330 335
 Arg Ala Gly Ala His Trp Ile Val Phe Ile Phe Leu Ile Leu Glu His
 340 345 350
 His His His His His
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<210> 827

<211> 96

<212> PRT

<213> Homo sapiens

<400> 827

Met Gly Ile Arg Glu Lys Phe Ala His Cys Thr Val Leu Thr Ile Ala
 5 10 15

His Arg Leu Asn Thr Ile Ile Asp Ser Asp Lys Ile Met Val Leu Asp
 20 25 30

006230"33219960

Ser Gly Arg Leu Lys Glu Tyr Asp Glu Pro Tyr Val Leu Leu Gln Asn
 35 40 45

Lys Glu Ser Leu Phe Tyr Lys Met Val Gln Gln Leu Gly Lys Ala Glu
 50 55 60

Ala Ala Ala Leu Thr Glu Thr Ala Lys Gln Arg Trp Gly Phe Thr Met
 65 70 75 80

Leu Ala Arg Leu Val Ser Asn Ser Leu Glu His His His His His His
 85 90 95

<210> 828

<211> 35

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer

<400> 828

cgcccatggg gatccgggag aaatttgccc actgc

35

<210> 829

<211> 35

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer

<400> 829

cgccctgagg gagtttgaga ccagcctggc caaca

35

<210> 830

<211> 38

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer

<400> 830

gcatggacca tatgtcagcc attgagaggg tgtcagag

38

<210> 831

<211> 34

<212> DNA

<213> Artificial Sequence

<220>

005230"3625360

<223> PCR primer

<400> 831

ccgctcgaga ataaggaaaa tgaagacaat ccag

34

<210> 832

<211> 27

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer

<400> 832

gttgaattca tgcacgggcc ccaggtg

27

<210> 833

<211> 30

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer

<400> 833

cccctcgagt cactatgggtc tgcctcttga

30

<210> 834

<211> 915

<212> DNA

<213> Homo sapiens

<400> 834

```

atgcatcacc atcaccatca cacggccgcg tccgataact tccagctgtc ccaggggtggg 60
cagggattcg ccattccgat cgggcaggcg atggcgatcg cgggccagat caagcttccc 120
accgttcata tcgggcctac cgccttcctc ggcttgggtg ttgtcgacaa caacggcaac 180
ggcgcacgag tccaacgcgt ggtcgggagc gctccggcgg caagtctcgg catctccacc 240
ggcgacgtga tcaccgcggg cgacggcgct ccgatcaact cggccaccgc gatggcggac 300
gcgcttaacg ggcacatccc cggtgacgtc atctcggtga cctggcaaac caagtccggc 360
ggcacgcgta cagggaaacgt gacattggcc gagggacccc cggccgaatt catgcacggg 420
ccccaggtgc tggcacgctg ctccgagtggt gcttgtcctg ccttggctgc cacctctgcg 480
ggggtgcgtc tggagggggg ggaccggcca ccaaccttac ccagtcaagg aagtggatgg 540
ccatgttccc acagcctgag tggctgccac ctgatggctg atggagcaaa ggccttagga 600
aaagcagatg gcccttggcc ctaccttttt gttagaagaa ctgatgttcc atgtcctgca 660
gogagtgagg ttggtggctg tgccccagc tcctggcgcg ccctcgcaga ggtgactggt 720
tgctcttttg gccctcttgg ccttgcccag catgcacaag cctcagtgtc actactgtgc 780
tacaaatgga gccatatagg ggaaacgagc agccatctca ggagcaagg gtatgtctgc 840
tttgggggct ccagtccttg cctcaagggt cttatgtcac tgtgggcttc ttggttgtca 900
agaggcagac catag                                     915

```

<210> 835

<211> 304

<212> PRT

<213> Homo sapiens

<400> 835

```

Met His His His His His His Thr Ala Ala Ser Asp Asn Phe Gln Leu
              5                      10                      15

Ser Gln Gly Gly Gln Gly Phe Ala Ile Pro Ile Gly Gln Ala Met Ala
              20                      25                      30

Ile Ala Gly Gln Ile Lys Leu Pro Thr Val His Ile Gly Pro Thr Ala
              35                      40                      45

Phe Leu Gly Leu Gly Val Val Asp Asn Asn Gly Asn Gly Ala Arg Val
              50                      55                      60

Gln Arg Val Val Gly Ser Ala Pro Ala Ala Ser Leu Gly Ile Ser Thr
              65                      70                      75                      80

Gly Asp Val Ile Thr Ala Val Asp Gly Ala Pro Ile Asn Ser Ala Thr
              85                      90                      95

Ala Met Ala Asp Ala Leu Asn Gly His His Pro Gly Asp Val Ile Ser
              100                     105                     110

Val Thr Trp Gln Thr Lys Ser Gly Gly Thr Arg Thr Gly Asn Val Thr
              115                     120                     125

Leu Ala Glu Gly Pro Pro Ala Glu Phe Met His Gly Pro Gln Val Leu
              130                     135                     140

Ala Arg Cys Ser Glu Cys Ala Cys Pro Ala Leu Ala Ala Thr Ser Ala
              145                     150                     155                     160

Gly Val Arg Leu Glu Gly Val Asp Arg Pro Pro Thr Leu Pro Ser Gln
              165                     170                     175

Gly Ser Gly Trp Pro Cys Ser His Ser Leu Ser Gly Cys His Leu Met
              180                     185                     190

Ala Asp Gly Ala Lys Ala Leu Gly Lys Ala Asp Gly Pro Trp Pro Tyr
              195                     200                     205

Leu Phe Val Arg Arg Thr Asp Val Pro Cys Pro Ala Ala Ser Glu Val
              210                     215                     220

Gly Gly Cys Ala Pro Ser Ser Trp Arg Ala Leu Ala Glu Val Thr Gly
              225                     230                     235                     240

Cys Ser Leu Gly Pro Leu Gly Leu Ala Gln His Ala Gln Ala Ser Val
              245                     250                     255

Leu Leu Leu Cys Tyr Lys Trp Ser His Ile Gly Glu Thr Ser Ser His

```

005220"32T360

260	265	270
Leu Arg Ser Lys Val Tyr Ala	Ala Phe Gly Gly Ser Ser	Pro Cys Leu
275	280	285
Lys Gly Leu Met Ser Leu Trp	Ala Ser Trp Leu Ser	Arg Gly Arg Pro
290	295	300

<210> 836
 <211> 24
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> PCR primer

<400> 836
 cgaagtcacg tggaggccag cctc 24

<210> 837
 <211> 29
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> PCR primer

<400> 837
 cctgaccgaa ttcattaact ggcttgac 29

<210> 838
 <211> 166
 <212> PRT
 <213> Homo sapiens

<220>
 <221> VARIANT
 <222> (1)...(166)
 <223> Xaa = Any Amino Acid

<400> 838
 Met Gly His His His His His Val Glu Ala Ser Leu Ser Val Arg
 1 5 10 15
 His Pro Glu Tyr Asn Arg Pro Leu Leu Ala Asn Asp Leu Met Leu Ile
 20 25 30
 Lys Leu Asp Glu Ser Val Ser Glu Ser Asp Thr Ile Arg Ser Ile Ser
 35 40 45
 Ile Ala Ser Gln Cys Pro Thr Ala Gly Asn Ser Cys Leu Val Ser Gly
 50 55 60
 Trp Gly Leu Leu Ala Asn Gly Arg Met Pro Thr Val Leu Gln Cys Val

006610"96696960

```

65          70          75          80
Asn Val Ser Val Val Ser Glu Glu Val Cys Ser Lys Leu Tyr Asp Pro
          85          90          95
Leu Tyr His Pro Ser Met Phe Cys Ala Gly Gly Gly Gln Xaa Gln Xaa
          100          105          110
Asp Ser Cys Asn Gly Asp Ser Gly Gly Pro Leu Ile Cys Asn Gly Tyr
          115          120          125
Leu Gln Gly Leu Val Ser Phe Gly Lys Ala Pro Cys Gly Gln Val Gly
          130          135          140
Val Pro Gly Val Tyr Thr Asn Leu Cys Lys Phe Thr Glu Trp Ile Glu
145          150          155          160
Lys Thr Val Gln Ala Ser
          165

```

<210> 839

<211> 504

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(504)

<223> n = A,T,C or G

<400> 839

```

atgggccatc atcatcatca tcacgtggag gccagcctct ccgtacggca cccagagtac      60
aacagaccct tgctcgctaa cgacctcatg ctcatcaagt tggacgaatc cgtgtccgag      120
tctgacacca tccggagcat cagcattgct tgcagtgcc ctaccgcggg gaactcttgc      180
ctcgtttctg gctggggtct gctggcgaac ggcagaatgc ctaccgtgct gcagtgcgtg      240
aacgtgtcgg tggtgtctga ggagggtctgc agtaagctct atgaccgct gtaccacccc      300
agcatgttct gcgccggcgg agggcaanac cagaangact cctgcaacgg tgactctggg      360
gggcccctga tctgcaacgg gtacttgacag ggccttggtgt ctttcggaaa agccccgtgt      420
ggccaagtgt gcgtgccagg tgtctacacc aacctctgca aattcactga gtggatagag      480
aaaaccgtcc aggccagtta atga                                     504

```

<210> 840

<211> 21

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer

<400> 840

```

ctcagggttc cggagccgcg g                                     21

```

<210> 841

<211> 35

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer

<400> 841
ctatagaatt cattaccaaa aagctgggct ccagc

35

<210> 842
<211> 241
<212> PRT
<213> Homo sapiens

<400> 842
Met Gln His His His His His Leu Arg Val Pro Glu Pro Arg Pro
1 5 10 15
Gly Glu Ala Lys Ala Glu Gly Ala Ala Pro Pro Thr Pro Ser Lys Pro
20 25 30
Leu Thr Ser Phe Leu Ile Gln Asp Ile Leu Arg Asp Gly Ala Gln Arg
35 40 45
Gln Gly Gly Arg Thr Ser Ser Gln Arg Gln Arg Asp Pro Glu Pro Glu
50 55 60
Pro Glu Pro Glu Pro Glu Gly Gly Arg Ser Arg Ala Gly Ala Gln Asn
65 70 75 80
Asp Gln Leu Ser Thr Gly Pro Arg Ala Ala Pro Glu Glu Ala Glu Thr
85 90 95
Leu Ala Glu Thr Glu Pro Glu Arg His Leu Gly Ser Tyr Leu Leu Asp
100 105 110
Ser Glu Asn Thr Ser Gly Ala Leu Pro Arg Leu Pro Gln Thr Pro Lys
115 120 125
Gln Pro Gln Lys Arg Ser Arg Ala Ala Phe Ser His Thr Gln Val Ile
130 135 140
Glu Leu Glu Arg Lys Phe Ser His Gln Lys Tyr Leu Ser Ala Pro Glu
145 150 155 160
Arg Ala His Leu Ala Lys Asn Leu Lys Leu Thr Glu Thr Gln Val Lys
165 170 175
Ile Trp Phe Gln Asn Arg Arg Tyr Lys Thr Lys Arg Lys Gln Leu Ser
180 185 190
Ser Glu Leu Gly Asp Leu Glu Lys His Ser Ser Leu Pro Ala Leu Lys
195 200 205
Glu Glu Ala Phe Ser Arg Ala Ser Leu Val Ser Val Tyr Asn Ser Tyr
210 215 220
Pro Tyr Tyr Pro Tyr Leu Tyr Cys Val Gly Ser Trp Ser Pro Ala Phe
225 230 235 240
Trp

<210> 843
<211> 729
<212> DNA
<213> Homo sapiens

<400> 843
atgcagcatc accaccatca ccacctcagg gttccggagc cgcggcccgg ggaggcgaaa 60
gcggaggggg ccgcgcgcc gaccccgctc aagccgctca cgtccttcct catccaggac 120
atcctgcggg acggcgcgca gcggcaaggc ggccgcacga gcagccagag acagcgcgac 180
ccggagccgg agccagagcc agagccagag ggaggacgca gccgcgccgg ggcgcagaaac 240

00630" 3E3E5E5E

```

gaccagctga gcaccggggcc ccgcgcgcgcg ccggatgagg ccgagacgct ggccagagacc 300
gagccagaaa ggcacttggg gtcttatctg ttggactctg aaaacacttc aggcgcctt 360
ccaaggcttc cccaaacccc taagcagccg cagaagcgct cccgagctgc cttctccac 420
actcaggtga tcgagttgga gaggaagttc agccatcaga agtacctgtc ggcccctgaa 480
cgggcccacc tggccaagaa cctcaagctc acggagaccc aagtgaagat atggttccag 540
aacagacgct ataagactaa gcgaaagcag ctctcctcgg agctgggaga cttggagaag 600
cactcctttt tgccggccct gaaagaggag gccttctccc gggcctccct ggtctccgtg 660
tataacagct atccttacta cccatacctg cactgcgtgg gcagctggag cccagctttt 720
tggtaatga 729

```

<210> 844

<211> 27

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer

<400> 844

ctactaagcg ctggagtggag ggatcag

27

<210> 845

<211> 33

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer

<400> 845

catcgagaat tcactactct ctgactagat gtc

33

<210> 846

<211> 161

<212> PRT

<213> Homo sapiens

<400> 846

```

Met Gln His His His His His Ala Gly Val Arg Asp Gln Gly Gln
 1          5          10          15
Gly Ala Arg Trp Pro His Thr Gly Lys Arg Gly Pro Leu Leu Gln Gly
 20          25          30
Leu Thr Trp Ala Thr Gly Gly His Cys Phe Ser Ser Glu Glu Ser Gly
 35          40          45
Ala Val Asp Gly Ala Gly Gln Lys Lys Asp Arg Ala Trp Leu Arg Cys
 50          55          60
Pro Glu Ala Val Ala Gly Phe Pro Leu Gly Ser Asp Cys Arg Glu Gly
 65          70          75          80
Gly Arg Gln Gly Cys Gly Gly Ser Asp Asp Glu Asp Asp Leu Gly Val
 85          90          95
Ala Pro Gly Leu Ala Pro Ala Trp Ala Leu Thr Gln Pro Pro Ser Gln

```

```

          100          105          110
Ser Pro Gly Pro Gln Ser Leu Pro Ser Thr Pro Ser Ser Ile Trp Pro
          115          120          125
Gln Trp Val Ile Leu Ile Thr Glu Leu Thr Ile Pro Ser Pro Ala His
          130          135          140
Gly Pro Pro Trp Leu Pro Asn Ala Leu Glu Arg Gly His Leu Val Arg
145          150          155          160
Glu

```

<210> 847

<211> 489

<212> DNA

<213> Homo sapiens

<400> 847

```

atgcagcatc accaccatca ccacgctgga gtgagggatc aggggcaggg cgcgagatgg      60
cctcacacag ggaagagagg gcccctcctg cagggcctca cctgggccac aggaggacac      120
tgcttttctt ctgaggagtc aggagctgtg gatgggtgctg gacagaagaa ggacagggcc      180
tggctcaggt gtccagaggc tgctcgtggc ttcccttttg gatcagactg cagggaggga      240
gggcggcagg gttgtggggg gagtgcacat gaggatgacc tgggggtggc tccaggcctt      300
gcccctgcct gggccctcac ccagcctccc tcacagtctc ctggccctca gtctctcccc      360
tccactccat cctccatctg gcctcagtgg gtcattctga tcaactgaact gaccataccc      420
agccctgccc acggccctcc atggctcccc aatgccctgg agaggggaca tctagtcaga      480
gagtagtga                                     489

```

<210> 848

<211> 132

<212> PRT

<213> Homo sapiens

<400> 848

```

Thr Ala Ala Ser Asp Asn Phe Gln Leu Ser Gln Gly Gly Gln Gly Phe
  1          5          10          15
Ala Ile Pro Ile Gly Gln Ala Met Ala Ile Ala Gly Gln Ile Arg Ser
          20          25          30
Gly Gly Gly Ser Pro Thr Val His Ile Gly Pro Thr Ala Phe Leu Gly
          35          40          45
Leu Gly Val Val Asp Asn Asn Gly Asn Gly Ala Arg Val Gln Arg Val
          50          55          60
Val Gly Ser Ala Pro Ala Ala Ser Leu Gly Ile Ser Thr Gly Asp Val
65          70          75          80
Ile Thr Ala Val Asp Gly Ala Pro Ile Asn Ser Ala Thr Ala Met Ala
          85          90          95
Asp Ala Leu Asn Gly His His Pro Gly Asp Val Ile Ser Val Asn Trp
          100          105          110
Gln Thr Lys Ser Gly Gly Thr Arg Thr Gly Asn Val Thr Leu Ala Glu
          115          120          125
Gly Pro Pro Ala
          130

```


<210> 849
 <211> 31
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> PCR primer

<400> 849
 ggggaattca tcacctatgt gccgcctctg c 31

<210> 850
 <211> 40
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> PCR primer

<400> 850
 gggctcgagt cactcgccca cgaaatccgt gtaaaacagc 40

<210> 851
 <211> 1203
 <212> DNA
 <213> Homo sapiens

<400> 851
 atgcatcacc atcaccatca cacggccgcg tccgataact tccagctgtc ccagggtggg 60
 cagggaattcg ccattccgat cgggcaggcg atggcgatcg cgggccagat caagcttccc 120
 accgttcata tcgggcctac cgccttcctc ggcttgggtg ttgtcgacaa caacggcaac 180
 ggcgacgtga tccaacgcgt ggtcgggagc gctccggcgg caagtctcgg catctccacc 240
 ggcgacgtga tcaccgcggt cgacggcgct ccgatcaact cggccaccgc gatggcggac 300
 gcgtttaacg ggcacatcc cgggtgacgt atctcggtga cctggcaaac caagtccggc 360
 ggcacgcgta cagggaacgt gacattggcc gagggacccc cggccgaatt catcacctat 420
 gtgccgcctc tgctgctgga agtgggggta gaggagaagt tcatgaccat ggtgctgggc 480
 attggtccag tgctgggcct ggtctgtgtc ccgctcctag gctcagccag tgaccactgg 540
 cgtggacgct atggccgcgc cggcccttc atctgggcac tgccttggg catcctgctg 600
 agcctctttc tcatcccaag ggccggctgg ctagcagggc tgctgtgccc ggatcccagg 660
 cccctggagc tggcactgct catcctgggc gtggggctgc tggacttctg tggccagggtg 720
 tgcttcactc cactggaggc cctgctctct gacctcttc gggacccgga ccactgtcgc 780
 caggcctact ctgtctatgc ctatcatgat agtcttgggg gctgcctggg ctacctcctg 840
 cctgccattg actgggacac cagtgcctcg gcccctacc tgggcaccca ggaggagtgc 900
 ctctttggcc tgctcaccct catcttcctc acctgcgtag cagccacact gctggtggct 960
 gaggaggcag cgctgggccc caccgagcca gcagaagggc tgtcggcccc ctcttgtcgc 1020
 cccactgct gtccatgccg ggcccgcttg gctttccgga acctgggcgc cctgcttccc 1080
 cggctgcacc agctgtgctg ccgcatgccc cgcacctgc gccggctctt cgtggctgag 1140
 ctgtgcagct ggatggcact catgaccttc acgtgtttt acacggattt cgtgggcgag 1200
 tga 1203

<210> 852
 <211> 400
 <212> PRT

<400> 852

Asp His Cys Arg Gln Ala Tyr Ser Val Tyr Ala Phe Met Ile Ser Leu
260 265 270

Ala Ser Ala Cys Asp Val Ser Val Arg Val
5 10

<210> 856
 <211> 30
 <212> DNA
 <213> Homo sapiens

<400> 856
 gcctctgcct gtgatgtctc cgtacgtgtg

30

<210> 857
 <211> 9
 <212> PRT
 <213> Homo sapiens

<400> 857
 Ala Ser Ala Cys Asp Val Ser Val Arg
 1 5

<210> 858
 <211> 9
 <212> PRT
 <213> Homo sapiens

<400> 858
 Ser Ala Cys Asp Val Ser Val Arg Val
 5

<210> 859
 <211> 27
 <212> DNA
 <213> Homo sapiens

<400> 859
 tctgcctgtg atgtctccgt acgtgtg

27

<210> 860
 <211> 19
 <212> PRT
 <213> Homo sapiens

<400> 860
 Gly Ile Gly Pro Val Leu Gly Leu Val Cys Val Pro Leu Leu Gly Ser
 5 10 15

Ala Ser Asp

<210> 861
 <211> 19
 <212> PRT
 <213> Homo sapiens

005230"9624590

<400> 861

Val Pro Pro Leu Leu Leu Glu Val Gly Val Glu Glu Lys Phe Met Thr
 5 10 15

Met Val Leu

<210> 862

<211> 19

<212> PRT

<213> Homo sapiens

<400> 862

Met Val Gln Arg Leu Trp Val Ser Arg Leu Leu Arg His Arg Lys Ala
 5 10 15

Gln Leu Leu

<210> 863

<211> 57

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(57)

<223> n = A,T,C or G

<400> 863

ggnathggnc cngtnytngg nytngtntgy gtncnnytny tnggnwsngc nwsngay 57

<210> 864

<211> 57

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(57)

<223> n = A,T,C or G

<400> 864

gtncncncny tnytnytnga rgtnggngtn gargaraart tyatgacnat ggtnytn 57

<210> 865

<211> 57

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

